FIGURE 1

Human DNase I

```
LOCUS       HUMDNASEI      1039 bp      mRNA           PRI       06-MAR-1995
DEFINITION  Human DNase I mRNA, complete cds.
ACCESSION   M55983
VERSION     M55983.1  GI:181623
KEYWORDS    DNase I.
SOURCE      Human pancreus, cDNA to mRNA.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
            Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1039)
  AUTHORS   Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE     Recombinant human DNase I reduces the viscosity of cystic fibrosis
            sputum
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE   91067672
FEATURES             Location/Qualifiers
     source          1..1039
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="hDNase-18-1"
                     /tissue_type="pancreas"
     sig peptide     160..225
                     /gene="DNase I"
     CDS             160..1008
                     /gene="DNase I"
                     /codon_start=1
                     /product="DNase I"
                     /protein_id="AAA63170.1"
                     /db_xref="GI:181624"
                     /translation="MRGMKLLGALLALAALLQGAVSLKIAAFNIQTFGETKMSNATLV
                     SYIVQILSRYDIALVQEVRDSHLTAVGKLLDNLNQDAPDTYHYVVSEPLGRNSYKERY
                     LFVYRPDQVSAVDSYYYDDGCEPCGNDTFNREPAIVRFFSRFTEVREFAIVPLHAAPG
                     DAVAEIDALYDVYLDVQEKWGLEDVMLMGDFNAGCSYVRPSQWSSIRLWTSPTFQWLI
                     PDSADTTATPTHCAYDRIVVAGMLLRGAVVPDSALPFNFQAAYGLSDQLAQAISDHYP
                     VEVMLK"
     gene            160..1008
                     /gene="DNase I"
     mat peptide     226..1005
                     /gene="DNase I"
                     /product="DNase I"
BASE COUNT      226 a     305 c     282 g     226 t
ORIGIN
        1 tcctgcacag gcagtgcctt gaagtgcttc ttcagagacc tttcttcata gactactttt
       61 ttttctttaa gcagcaaaag gagaaaattg tcatcaaagg atattccaga ttcttgacag
      121 cattctcgtc atctctgagg acatcaccat catctcagga tgaggggcat gaagctgctg
      181 ggggcgctgc tggcactggc ggccctactg caggggggcg tgtccctgaa gatcgcagcc
      241 ttcaacatcc agacatttgg ggagaccaag atgtccaatg ccaccctcgt cagctacatt
      301 gtgcagatcc tgagccgcta tgacatcgcc ctggtccagg aggtcagaga cagccacctg
      361 actgccgtgg ggaagctgct ggacaacctc aatcaggatg caccagacac ctatcactac
      421 gtggtcagtg agccactggg acggaacagc tataaggagc gctacctgtt cgtgtacagg
      481 cctgaccagg tgtctgcggt ggacagctac tactacgatg atggctgcga gccctgcggg
      541 aacgacacct caaccgagag ccagccatt  gtcaggttct ctccgggtt  cacagaggtc
      601 agggagtttg ccattgttcc cctgcatgcg gccccggggg acgcagtagc cgagatcgac
      661 gctctctatg acgtctacct ggatgtccaa gagaaatggg gcttggagga cgtcatgttg
      721 atgggcgact tcaatgcggg ctgcagctat gtgagaccct cccagtggtc atccatccgc
      781 ctgtggacaa gccccacctt ccagtggctg atccccgaca gcgctgacac cacagctaca
      841 cccacgcact gtgcctatga caggatcgtg gttgcaggga tgctgctccg aggcgccgtt
      901 gtt··cgact cggctcttcc ctttaacttc caggctgcct atggcctgag tgaccaactg
      961 gcccaagcca tcagtgacca ctatccagtg gaggtgatgc tgaagtgagc agccctccc
     1021 cacaccagtt gaactgcag
//
```

FIGURE 2   human DNAse I construct

(A)

```
LOCUS        MHDNASE.DN   783 bp     mRNA              PRI      06-MAR-1995
DEFINITION   Human DNase I mRNA, complete cds, Mature sequence modified to remove NarI site
ACCESSION    M55983
NID          g181623
KEYWORDS     DNase I.
SOURCE       Human pancreus, cDNA to mRNA.
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE    1  (bases 1 to 1039)
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
FEATURES             Location/Qualifiers
     source          1. .1039
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="hDNase-18-1"
                     /tissue_type="pancreas"
     sig_peptide     160. .225
                     /gene="DNase I"
     CDS             160. .1008
                     /gene="DNase I"
                     /codon_start=1
                     /product="DNase I"
                     /db_xref="PID:g181624"
                     /translation="LKIAAFNIQTFGETKMSNATLVSYIVQILSRYDIALVQEVRDSH
                     LTAVGKLLDNLNQDAPDTYHYVVSEPLGRNSYKERYLFVYRPDQVSAVDSYYYDDGCE
                     PCGNDTFNREPAIVRFFSRFTEVREFAIVPLHAAPGDAVAEIDALYDVYLDVQEKWGL
                     EDVMLMGDFNAGCSYVRPSQWSSIRLWTSPTFQWLIPDSADTTATPTHCAYDRIVVAG
                     MLLRGAVVPDSALPFNFQAAYGLSDQLAQAISDHYPVEVMLK"
     gene            160. .1008
                     /gene="DNase I"
     mat_peptide     226. .1005
                     /gene="DNase I"
                     /product="DNase I"
BASE COUNT      168 a    236 c    220 g    159 t
ORIGIN
        1 CTGAAGATCG CAGCCTTCAA CATCCAGACA TTTGGGGAGA CCAAGATGTC CAATGCCACC
       61 CTCGTCAGCT ACATTGTGCA GATCCTGAGC CGCTACGACA TCGCCCTGGT CCAGGAGGTC
      121 AGAGACAGCC ACCTGACTGC CGTGGGGAAG CTGCTGGACA ACCTCAATCA GGACGCACCA
      181 GACACCTATC ACTACGTGGT CAGTGAGCCA CTGGGACGGA ACAGCTATAA GGAGCGCTAC
      241 CTGTTCGTGT ACAGGCCTGA CCAGGTGTCT GCGGTGGACA GCTACTACTA CGATGATGGC
      301 TGCGAGCCCT GCGGGAACGA CACCTTCAAC CGAGAGCCAG CCATTGTCAG GTTCTTCTCC
      361 CGGTTCACAG AGGTCAGGGA GTTTGCCATT GTTCCCCTGC ATGCGGCCCC GGGGGACGCA
      421 GTAGCCGAGA TCGACGCTCT CTATGACGTC TACCTGGATG TCCAAGAGAA ATGGGGCTTG
      481 GAGGACGTCA TGTTGATGGG CGACTTCAAT GCGGGCTGCA GCTATGTGAG ACCCTCCCAG
      541 TGGTCATCCA TCCGCCTGTG GACAAGCCCC ACCTTCCAGT GGCTGATCCC CGACAGCGCT
      601 GACACCACAG CTACACCCAC GCACTGTGCC TATGACAGGA TCGTGGTTGC AGGGATGCTG
      661 CTCCGAGGGG CCGTTGTTCC CGACTCGGCT CTTCCCTTTA ACTTCCAGGC TGCCTATGGC
      721 CTGAGTGACC AACTGGCCCA AGCCATCAGT GACCACTATC CAGTGGAGGT GATGCTGAAG
      781 TGA
//
```

FIGURE 2(B)

```
LOCUS       PAS155_GB.    858 BP SS-DNA              SYN        29-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES              Location/Qualifiers
     frag            10..75
                     /note="160 to 225 of Untitled1"
     frag            <10..>75
                     /note="1 to 1039 of M55983.DNA [Split]"
     source          <10..>75
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="hDNase-18-1"
                     /tissue_type="pancreas [Split]"
     sig_peptide     10..75
                     /gene="DNase I"
     CDS             10..>75
                     /gene="DNase I"
                     /codon_start="1"
                     /product="DNase I"
                     /db_xref="PID:g181624"
                     /translation="MRGMKLLGALLALAALLQGAVSLKIAAFNIQTFGETKMSNATLV
                     SYIVQILSRYDIALVQEVRDSHLTAVGKLLDNLNQDAPDTYHYVVSEPLGRNSYKERY
                     LFVYRPDQVSAVDSYYYDDGCEPCGNDTFNREPAIVRFFSRFTEVREFAIVPLHAAPG
                     D... [Split]"
     gene            10..>75
                     /gene="DNase I [Split]"
     frag            76..858
                     /note="1 to 783 of mod humanDNAseI"
     frag            76..858
                     /note="1 to 72 of 104linker"
     frag            join(76..>129,<131..147)
                     /note="1 to 72 of 103linker [Split]"
     frag            join(76..>126,<127..>129,<131..147)
                     /note="1 to 78 of 102linker [Split]"
BASE COUNT      177 A     260 C    251 G     170 T        0 OTHER
ORIGIN      -
        1 GCCGCCACCA TGAGGGGCAT GAAGCTGCTG GGGGCGCTGC TGGCACTGGC GGCCCTACTG
       61 CAGGGGGCCG TGTCCCTGAA GATCGCAGCC TTCAACATCC AGACATTTGG GGAGACCAAG
      121 ATGTCCAATG CCACCCTCGT CAGCTACATT GTGCAGATCC TGAGCCGCTA CGACATCGCC
      181 CTGGTCCAGG AGGTCAGAGA CAGCCACCTG ACTGCCGTGG GGAAGCTGCT GGACAACCTC
      241 AATCAGGACG CACCAGACAC CTATCACTAC GTGGTCAGTG AGCCACTGGG ACGGAACAGC
      301 TATAAGGAGC GCTACCTGTT CGTGTACAGG CCTGACCAGG TGTCTGCGGT GGACAGCTAC
      361 TACTACGATG ATGGCTGCGA GCCCTGCGGG AACGACACCT TCAACCGAGA GCCAGCCATT
      421 GTCAGGTTCT TCTCCCGGTT CACAGAGGTC AGGGAGTTTG CCATTGTTCC CCTGCATGCG
      481 GCCCCGGGGG ACGCAGTAGC CGAGATCGAC GCTCTCTATG ACGTCTACCT GGATGTCCAA
      541 GAGAAATGGG GCTTGGAGGA CGTCATGTTG ATGGGCGACT TCAATGCGGG CTGCAGCTAT
      601 GTGAGACCCT CCCAGTGGTC ATCCATCCGC CTGTGGACAA GCCCCACCTT CCAGTGGCTG
      661 ATCCCCGACA GCGCTGACAC CACAGCTACA CCCACGCACT GTGCCTATGA CAGGATCGTG
      721 GTTGCAGGGA TGCTGCTCCG AGGGGCCGTT GTTCCCGACT CGGCTCTTCC CTTTAACTTC
      781 CAGGCTGCCT ATGGCCTGAG TGACCAACTG GCCCAAGCCA TCAGTGACCA CTATCCAGTG
      841 GAGGTGATGC TGAAGTGA
```

FIGURE 3

(A)   pAS6 - light chain

```
LOCUS       HMFG1LC2.D    721 bp    DNA
DEFINITION  HUMANISED HMFG1 LIGHT CHAIN Vnp LEADER.
ACCESSION .
KEYWORDS
SOURCE
  ORGANISM
REFERENCE   1  (BASES 1 TO 342)
  AUTHORS   VERHOEYEN ET AL
  TITLE     CONSTRUCTION OF RESHAPED HMFG1 ETC
  JOURNAL   IMMUNOL. (1993):78, 364-370
COMMENT     SCANNED IN FROM JOURNAL
FEATURES
  SITES
```

This is the sequence of the HMFG1 light chain gene with the
Vnp leader sequence attached. Translate from
residue 1. Note residue 399 is T > A in all clones leading
to R133 silent mutation (T in Verhoeyen paper)

```
BASE COUNT       197 a     202 c     162 g     140 t
ORIGIN           ?                LEADER SEQ
     1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCGAC
    61 ATCCAGATGA CCCAGAGCCC AAGCAGCCTG AGCGCCAGCG TGGGTGACAG AGTGACCATC
   121 ACCTGTAAGT CCAGTCAGAG CCTTTTATAT AGTAGCAATC AAAAGATCTA CTTGGCCTGG
   181 TACCAGCAGA AGCCAGGTAA GGCTCCAAAG CTGCTGATCT ACTGGGCATC CACTAGGGAA
   241 TCTGGTGTGC CAAGCAGATT CAGCGGTAGC GGTAGCGGTA CCGACTTCAC CTTCACCATC
   301 AGCAGCCTCC AGCCAGACGA CATCGCCACC TACTACTGCC AGCAATATTA TAGATATCCT
   361 CGGACGTTCG GCCAAGGGAC CAAGGTGGAA ATCAAACGAA CTGTGGCTGC ACCATCTGTC
   421 TTCATCTTCC CGCCATCTGA TGAGCAGTTG AAATCTGGAA CTGCCTCTGT TGTGTGCCTG
   481 CTGAATAACT TCTATCCCAG AGAGGCCAAA GTACAGTGGA AGGTGGATAA CGCCCTCCAA
   541 TCGGGTAACT CCCAGGAGAG TGTCACAGAG CAGGACAGCA AGGACAGCAC CTACAGCCTC
   601 AGCAGCACCC TGACGCTGAG CAAAGCAGAC TACGAGAAAC ACAAAGTCTA CGCCTGCGAA
   661 GTCACCCATC AGGGCCTGAG CTCGCCCGTC ACAAAGAGCT TCAACAGGGG AGAGTGTTAG
   721 A
//
```

4/113

Figure 3(B)

```
LOCUS       HHMFG1KLC_      730 BP SS-DNA              SYN        29-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES                Location/Qualifiers
     frag               10..730
                        /note="1 to 721 of hHMFG1light chain"
     frag               10..730
                        /note="1 to 72 of 104linker"
     frag               join(10..>63,<65..81)
                        /note="1 to 72 of 103linker [Split]"
     frag               join(10..>60,<61..>63,<65..81)
                        /note="1 to 78 of 102linker [Split]"
 ''SE COUNT      198 A      208 C      184 G      140 T        0 OTHER
 .''IGIN     -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCGACA TCCAGATGAC CCAGAGCCCA AGCAGCCTGA GCGCCAGCGT GGGTGACAGA
      121 GTGACCATCA CCTGTAAGTC CAGTCAGAGC CTTTTATATA GTAGCAATCA AAAGATCTAC
      181 TTGGCCTGGT ACCAGCAGAA GCCAGGTAAG GCTCCAAAGC TGCTGATCTA CTGGGCATCC
      241 ACTAGGGAAT CTGGTGTGCC AAGCAGATTC AGCGGTAGCG GTAGCGGTAC CGACTTCACC
      301 TTCACCATCA GCAGCCTCCA GCCAGAGGAC ATCGCCACCT ACTACTGCCA GCAATATTAT
      361 AGATATCCTC GGACGTTCGG CCAAGGGACC AAGGTGGAAA TCAAACGAAC TGTGGCTGCA
      421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCCTCTGTT
      481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
      541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
      601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
      661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
      721 GAGTGTTAGA
//
```

Figure 3 (c)

HMFG-1 light chain with Vnp Leader (shaded)

MGWSCIILFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCKSSQSL
LYSSNQKIYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGT
DFTFTISSLQPEDIATYYCQQYYRYPRTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESV
TEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC

FIGURE 3

(D) pAS6 - heavy chain

```
LOCUS        HHMFG1HC.D    1404 bp      DNA
DEFINITION   HUMANISED HMFG1 heavy chain
ACCESSION    HHMFG1H
KEYWORDS
SOURCE
  ORGANISM
REFERENCE
  AUTHORS    VERHOEYEN ET AL
  TITLE      CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL    IMMUNOL. (1993):78, 364-370
COMMENT      VH domain SCANNED IN FROM JOURNAL
FEATURES     AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES     Residue 963 is G > T leading to silent mutation in all clones
  SITES      Note
BASE COUNT      333 a     439 c     379 g     253 t
ORIGIN          ?
```

← LEADER →

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAAGTCACT AGAGACAGAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT CCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CTCCGGGTAA ATGA
```

▲ ANTIBODY DNAse FUSIONS MADE HERE (eg pAS 34→39.)

➤ End of lower hinge region of HEAVY CHAIN. PAPE Amino Acid SEQ. Fab'₂ Fusions were Made at this point.

Those with HYBRID HINGES ARE ALTERED FURTHER up

↙ ie.

➤ THIS PART GACAAAACTGACACA
   is →   D   K   T H T

AFTER THIS SEQVENCE YOU GET THE
HYBRID HINGE + LINKER SEQUENCES
Then DNAse I (eg Fab-DNase construct pAS302)

FIGURE 4

(A.) Oligos involved in the fusion of whole antibody-DNase

Constructs pAS34/37

AS79
AS80

			CCG	GGT	AAA	GGG	AGC	GGC	GGG	CTG	AAG	ATC	GCA	GCC	TTC	AAC
GAG	AGG	GAC	AGA	GGC	CCA	CCC	TCG	CCG	CCC		GAC	TTC	TAG				
L	S	L	S	P	G	K	G	S	G	G	L	K	I	A	A	F	N

HMFG1   LINKER   hu DNase I

Constructs pAS35/38

AS81
AS82

			CCG	AAA	GGG	AGC	GGC	GGG	CTG	AAG	ATC	GCA	GCC	TTC	AAC
GAG	AGG	GAC	AGA	GGC	TTT	CCC	TCG	CCG	CCC		GAC	TTC	TAG				
L	S	L	S	P	K	G	S	G	G	L	K	I	A	A	F	N

HMFG1   ΔG (deletion)   LINKER   hu DNase I

Constructs pAS36/39

AS83
AS84

			CCG	GGG	AGC	GGC	GGG	CTG	AAG	ATC	GCA	GCC	TTC	AAC
GAG	AGG	GAC	AGA	GGC	CCC	TCG	CCG	CCC		GAC	TTC	TAG				
L	S	L	S	P	G	S	G	G	L	K	I	A	A	F	N

HMFG1   ΔG (deletion)   LINKER   hu DNase I

Oligos involved in the fusion of Fab'2-DNaseI

Constructs pAS23/27

AS73
AS74

	GCA	CCT	GAA	GGG	AGC	GGC	GGG	CTG	AAG	ATC	GCA	GCC	TTC	AAC
GGT	GGC	ACG	GGT	CGT	GGA	CTT	CCC	TCG	CCG	CCC		GAC	TTC	TAG				
P	P	C	P	A	P	E	G	S	G	G	L	K	I	A	A	F	N

HMFG1 HINGE   LINKER   hu DNase I

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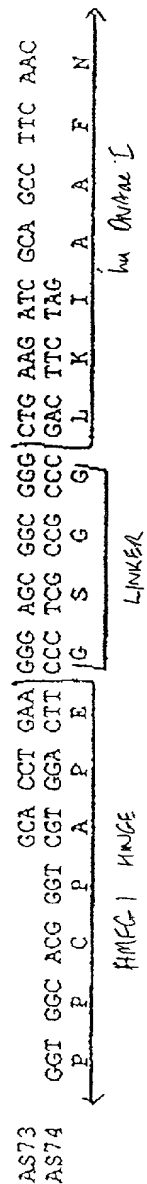
FIGURE 4

(b) Oligos involved in the fusion of new Fab'2-DNaseI molecules (5.7.99)

Constructs pAS101/105

```
AS86
AS87
                GCA CCT GAA|GGC GGG|CTG AAG ATC GCA GCC TTC AAC
        GGT GGC ACG GGT CGT CCG CTT GGA|CCG CCC|GAC TTC TAG
         P   P   C   P   A   P   E |G   G |L   K   I   A   A   F   N
        |_____|      |_____|
              HMFG1 (hinge)         SHORT      hu DNase I
                                   LINKER
```

Constructs pAS102/106

```
AS88
AS89
                        GAG TGT CCA CCG TGT CCA GCA CCA GAG|GGG AGC GGC GGG|CTG AAG ATC GCA GCC TTC
        CTG TTT TGA GTG TGT|ACG ACA CAG GAG CTC ACA GGT CGT GGC CTC|CCC TCG|GAC TTC TAG
         D   K   T   H   T | C   C   V   E   C   P   P   C   P   A   P   E |G   S   G   G |L   K   I   A   A   F
        |_____| |_____|            |_____|
             HMFG1                        HYBRID HINGE                      LONG LINKER      hu DNase I
```

Constructs pAS103/107

```
AS90
AS91
                        GTC GAG TGT CCA CCG TGT CCA GCA CCA GAG|GGC GGG|CTG AAG ATC GCA GCC TTC
        CTG TTT TGA GTG TGT|ACG ACA CAG GAG CTC ACA GGT CGT GGC CTC|CCG|GAC TTC TAG
         D   K   T   H   T | C   C   V   E   C   P   P   C   P   A   P   E |G   G |L   K   I   A   A   F
        |_____| |_____|        |_____|
             HMFG1                        HYBRID HINGE                      SHORT         hu DNase I
                                                                           LINKER
```

FIGURE 5.

(A) pAS23

```
LOCUS       PAS23.DNA    1554 bp     mRNA              PRI        06-MAR-1995
DEFINITION  Humanised HMFG1 Fab'2 fused to human DNase I (construct 1)
ACCESSION
NID
KEYWORDS    DNase I.
SOURCE      DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS   Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE     Recombinant human DNase I reduces the viscosity of cystic fibrosis
            sputum
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE   91067672
BASE COUNT      344 a    468 c    434 g    308 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAG GGAGCGGCGG GCTGAAGATC
 781 GCAGCCTTCA ACATCCAGAC ATTTGGGGAG ACCAAGATGT CCAATGCCAC CCTCGTCAGC
 841 TACATTGTGC AGATCCTGAG CCGCTACGAC ATCGCCCTGG TCCAGGAGGT CAGAGACAGC
 901 CACCTGACTG CCGTGGGGAA GCTGCTGGAC AACCTCAATC AGGACGCACC AGACACCTAT
 961 CACTACGTGG TCAGTGAGCC ACTGGGACGG AACAGCTATA AGGAGCGCTA CCTGTTCGTG
1021 TACAGGCCTG ACCAGGTGTC TGCGGTGGAC AGCTACTACT ACGATGATGG CTGCGAGCCC
1081 TGCGGGAACG ACACCTTCAA CCGAGAGCCA GCCATTGTCA GGTTCTTCTC CCGGTTCACA
1141 GAGGTCAGGG AGTTTGCCAT TGTTCCCCTG CATGCGGCCC CGGGGGACGC AGTAGCCGAG
1201 ATCGACGCTC TCTATGACGT CTACCTGGAT GTCCAAGAGA ATGGGGCTT GGAGGACGTC
1261 ATGTTGATGG CGACTTCAA TGCGGGCTGC AGCTATGTGA GACCCTCCCA GTGGTCATCC
1321 ATCCGCCTGT GGACAAGCCC CACCTTCCAG TGGCTGATCC CCGACAGCGC TGACACCACA
1381 GCTACACCCA CGCACTGTGC CTATGACAGG ATCGTGGTTG CAGGGATGCT GCTCCGAGGG
1441 GCCGTTGTTC CCGACTCGGC TCTTCCCTTT AACTTCCAGG CTGCCTATGG CCTGAGTGAC
1501 CAACTGGCCC AAGCCATCAG TGACCACTAT CCAGTGGAGG TGATGCTGAA GTGA
//
```

Figure 5 (B)

```
LOCUS        FDDNASE23_   1554 BP SS-DNA            SYN        25-AUG-2000
DEFINITION   -
ACCESSION    -
KYWORDS      -
SOURCE       -
FEATURES                 Location/Qualifiers
     frag                join(1..>720,<787..1554)
                         /note="1 to 1554 of 23.dna [Split]"
     frag                721..786
                         /note="1 to 66 of 23/27linker"
     frag                join(721..>735,<736..786)
                         /note="1 to 78 of 102linker [Split]"
BASE COUNT      344 A     466 C     435 G     309 T       0 OTHER
ORIGIN       -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACGGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGTCC ACCGTGTCCA GCACCAGAGG GGAGCGGCGG GCTGAAGATC
      781 GCAGCCTTCA ACATCCAGAC ATTTGGGGAG ACCAAGATGT CCAATGCCAC CCTCGTCAGC
      841 TACATTGTGC AGATCCTGAG CCGCTACGAC ATCGCCCTGG TCCAGGAGGT CAGAGACAGC
      901 CACCTGACTG CCGTGGGGAA GCTGCTGGAC AACCTCAATC AGGACGCACC AGACACCTAT
      961 CACTACGTGG TCAGTGAGCC ACTGGGACGG AACAGCTATA AGGAGCGCTA CCTGTTCGTG
     1021 TACAGGCCTG ACCAGGTGTC TGCGGTGGAC AGCTACTACT ACGATGATGG CTGCGAGCCC
     1081 TGCGGGAACG ACACCTTCAA CCGAGAGCCA GCCATTGTCA GGTTCTTCTC CCGGTTCACA
     1141 GAGGTCAGGG AGTTTGCCAT TGTTCCCCTG CATGCGGCCC CGGGGGACGC AGTAGCCGAG
     1201 ATCGACGCTC TCTATGACGT CTACCTGGAT GTCCAAGAGA AATGGGGCTT GGAGGACGTC
     1261 ATGTTGATGG GCGACTTCAA TGCGGGCTGC AGCTATGTGA GACCCTCCCA GTGGTCATCC
     1321 ATCCGCCTGT GGACAAGCCC CACCTTCCAG TGGCTGATCC CCGACAGCGC TGACACCACA
     1381 GCTACACCCA CGCACTGTGC CTATGACAGG ATCGTGGTTG CAGGGATGCT GCTCCGAGGG
     1441 GCCGTTGTTC CGGACTCGGC TCTTCCCTTT AACTTCCAGG CTGCCTATGG CCTGAGTGAC
     1501 CAACTGGCCC AAGCCATCAG TGACCACTAT CCAGTGGAGG TGATGCTGAA GTGA
//
```

Figure 5 (c)

```
 CUS       FDDNASE23K   1563 BP SS-DNA           SYN        29-AUG-2000
 CFINITION   -
 CCESSION    -
 YWORDS      -
SOURCE        -
FEATURES               Location/Qualifiers
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                       /note="1 to 1554 of FdDNase23correct"
     frag              join(10..>729,<796..1563)
                       /note="1 to 1554 of 23.dna [Split]"
     frag              730..795
                       /note="1 to 66 of 23/27linker"
     frag              join(730..>744,<745..795)
                       /note="1 to 78 of 102linker [Split]"
BASE COUNT      345 A     472 C     437 G     309 T        0 OTHER
ORIGIN        -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGTCCA CCGTGTCCAG CACCAGAGGG GAGCGGCGGG
      781 CTGAAGATCG CAGCCTTCAA CATCCAGACA TTTGGGGAGA CCAAGATGTC CAATGCCACC
      841 CTCGTCAGCT ACATTGTGCA GATCCTGAGC CGCTACGACA TCGCCCTGGT CCAGGAGGTC
      901 AGAGACAGCC ACCTGACTGC CGTGGGGAAG CTGCTGGACA ACCTCAATCA GGACGCACCA
      961 GACACCTATC ACTACGTGGT CAGTGAGCCA CTGGGACGGA ACAGCTATAA GGAGCGCTAC
     1021 CTGTTCGTGT ACAGGCCTGA CCAGGTGTCT GCGGTGGACA GCTACTACTA CGATGATGGC
     1081 TGCGAGCCCT GCGGGAACGA CACCTTCAAC CGAGAGCCAG CCATTGTCAG GTTCTTCTCC
     1141 CGGTTCACAG AGGTCAGGGA GTTTGCCATT GTTCCCCTGC ATGCGGCCCC GGGGGACGCA
     1201 GTAGCCGAGA TCGACGCTCT CTATGACGTC TACCTGGATG TCCAAGAGAA ATGGGGCTTG
     1261 GAGGACGTCA TGTTGATGGG CGACTTCAAT GCGGGCTGCA GCTATGTGAG ACCCTCCCAG
     1321 TGGTCATCCA TCCGCCTGTG GACAAGCCCC ACCTTCCAGT GGCTGATCCC CGACAGCGCT
     1381 GACACCACAG CTACACCCAC GCACTGTGCC TATGACAGGA TCGTGGTTGC AGGGATGCTG
     1441 CTCCGAGGGG CCGTTGTTCC CGACTCGGCT CTTCCCTTTA ACTTCCAGGC TGCCTATGGC
     1501 CTGAGTGACC AACTGGCCCA AGCCATCAGT GACCACTATC CAGTGGAGGT GATGCTGAAG
     1561 TGA
//
```

```
                9          18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


                63         72          81          90          99          108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


                117        126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


                171        180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


                225        234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


                279        288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


                333        342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


                387        396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


                441        450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


                495        504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


                549        558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

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```
        603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

        657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

        765         774         783         792         801         810
GAA GGG AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   G   S   G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E

        819         828         837         846         855         864
ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R

        873         882         891         900         909         918
TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Y   D   I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G

        927         936         945         954         963         972
AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 K   L   L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V

        981         990         999        1008        1017        1026
AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   E   P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R

       1035        1044        1053        1062        1071        1080
CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P

       1089        1098        1107        1116        1125        1134
TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   G   N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R

       1143        1152        1161        1170        1179        1188
TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   T   E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D

       1197        1206        1215        1224        1233        1242
```

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```
GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   V   A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K

      1251        1260        1269        1278        1287        1296
TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 W   G   L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y

      1305        1314        1323        1332        1341        1350
GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   R   P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q

      1359        1368        1377        1386        1395        1404
TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 W   L   I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y

      1413        1422        1431        1440        1449        1458
GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   R   I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S

      1467        1476        1485        1494        1503        1512
GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q

      1521        1530        1539        1548
GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
--- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   I   S   D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 6

(A) pAS27

```
LOCUS        PAS27.DNA     1584 bp      mRNA            PRI         06-MAR-1995
DEFINITION   Humanised HMFG1 Fab'2 fused to human DNase I with SV40 NLS(construct
1)
ACCESSION
NID
KEYWORDS     DNase I.
SOURCE       DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
BASE COUNT      354 a     474 c     446 g     310 t
ORIGIN
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```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAG GGAGCGGCGG GCTGAAGATC
 781 GCAGCCTTCA ACATCCAGAC ATTTGGGGAG ACCAAGATGT CCAATGCCAC CCTCGTCAGC
 841 TACATTGTGC AGATCCTGAG CCGCTACGAC ATCGCCCTGG TCCAGGAGGT CAGAGACAGC
 901 CACCTGACTG CCGTGGGGAA GCTGCTGGAC AACCTCAATC AGGACGCACC AGACACCTAT
 961 CACTACGTGG TCAGTGAGCC ACTGGGACGG AACAGCTATA AGGAGCGCTA CCTGTTCGTG
1021 TACAGGCCTG ACCAGGTGTC TGCGGTGGAC AGCTACTACT ACGATGATGG CTGCGAGCCC
1081 TGCGGGAACG ACACCTTCAA CCGAGAGCCA GCCATTGTCA GGTTCTTCTC CCGGTTCACA
1141 GAGGTCAGGG AGTTTGCCAT TGTTCCCCTG CATGCGGCCC CGGGGGACGC AGTAGCCGAG
1201 ATCGACGCTC TCTATGACGT CTACCTGGAT GTCCAAGAGA AATGGGGCTT GGAGGACGTC
1261 ATGTTGATGG GCGACTTCAA TGCGGGCTGC AGCTATGTGA GACCCTCCCA GTGGTCATCC
1321 ATCCGCCTGT GGACAAGCCC CACCTTCCAG TGGCTGATCC CCGACAGCGC TGACACCACA
1381 GCTACACCCA CGCACTGTGC CTATGACAGG ATCGTGGTTG CAGGGATGCT GCTCCGAGGG
1441 GCCGTTGTTC CCGACTCGGC TCTTCCCTTT AACTTCCAGG CTGCCTATGG CCTGAGTGAC
1501 CAACTGGCCC AAGCCATCAG TGACCACTAT CCAGTGGAGG TGATGCTGAA GGGGGGCGGA
1561 CCCAAAAAGA AGCGCAAGGT TTGA
```

//

└→ NLS

Figure 6 (B)

```
LOCUS      FDDNASE27_  1584 BP SS-DNA          SYN        25-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES              Location/Qualifiers
     frag             join(1..>720,<787..1584)
                      /note="1 to 1584 of 27.dna [Split]"
     frag             721..786
                      /note="1 to 66 of 23/27linker"
     frag             join(721..>735,<736..786)
                      /note="1 to 78 of 102linker [Split]"
BASE COUNT     354 A    472 C    447 G    311 T      0 OTHER
ORIGIN      -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGTCC ACCGTGTCCA GCACCAGAGG GGAGCGGCGG GCTGAAGATC
      781 GCAGCCTTCA ACATCCAGAC ATTTGGGGAG ACCAAGATGT CCAATGCCAC CCTCGTCAGC
      841 TACATTGTGC AGATCCTGAG CCGCTACGAC ATCGCCCTGG TCCAGGAGGT CAGAGACAGC
      901 CACCTGACTG CCGTGGGGAA GCTGCTGGAC AACCTCAATC AGGACGCACC AGACACCTAT
      961 CACTACGTGG TCAGTGAGCC ACTGGGACGG AACAGCTATA AGGAGCGCTA CCTGTTCGTG
     1021 TACAGGCCTG ACCAGGTGTC TGCGGTGGAC AGCTACTACT ACGATGATGG CTGCGAGCCC
     1081 TGCGGGAACG ACACCTTCAA CCGAGAGCCA GCCATTGTCA GGTTCTTCTC CCGGTTCACA
     1141 GAGGTCAGGG AGTTTGCCAT TGTTCCCCTG CATGCGGCCC CGGGGGACGC AGTAGCCGAG
     1201 ATCGACGCTC TCTATGACGT CTACCTGGAT GTCCAAGAGA AATGGGGCTT GGAGGACGTC
     1261 ATGTTGATGG GCGACTTCAA TGCGGGCTGC AGCTATGTGA GACCCTCCCA GTGGTCATCC
     1321 ATCCGCCTGT GGACAAGCCC CACCTTCCAG TGGCTGATCC CCGACAGCGC TGACACCACA
     1381 GCTACACCCA CGCACTGTGC CTATGACAGG ATCGTGGTTG CAGGGATGCT GCTCCGAGGG
     1441 GCCGTTGTTC CCGACTCGGC TCTTCCCTTT AACTTCCAGG CTGCCTATGG CCTGAGTGAC
     1501 CAACTGGCCC AAGCCATCAG TGACCACTAT CCAGTGGAGG TGATGCTGAA GGGGGGCGGA
     1561 CCCAAAAAGA AGCGCAAGGT TTGA
//
```

Figure 6(c)

```
LOCUS       FDDNASE27K   1593 BP SS-DNA        SYN        29-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES              Location/Qualifiers
        frag          10..1593
                      /note="1 to 1584 of FdDNase27correct"
        frag          join(10..>729,<796..1593)
                      /note="1 to 1584 of 27.dna [Split]"
        frag          730..795
                      /note="1 to 66 of 23/27linker"
        frag          join(730..>744,<745..795)
                      /note="1 to 78 of 102linker [Split]"
BASE COUNT      355 A    478 C    449 G    311 T       0 OTHER
ORIGIN       -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGTCCA CCGTGTCCAG CACCAGAGGG GAGCGGCGGG
      781 CTGAAGATCG CAGCCTTCAA CATCCAGACA TTTGGGGAGA CCAAGATGTC CAATGCCACC
      841 CTCGTCAGCT ACATTGTGCA GATCCTGAGC CGCTACGACA TCGCCCTGGT CCAGGAGGTC
      901 AGAGACAGCC ACCTGACTGC CGTGGGGAAG CTGCTGGACA ACCTCAATCA GGACGCACCA
      961 GACACCTATC ACTACGTGGT CAGTGAGCCA CTGGGACGGA ACAGCTATAA GGAGCGCTAC
     1021 CTGTTCGTGT ACAGGCCTGA CCAGGTGTCT GCGGTGGACA GCTACTACTA CGATGATGGC
     1081 TGCGAGCCCT GCGGGAACGA CACCTTCAAC CGAGAGCCAG CCATTGTCAG GTTCTTCTCC
     1141 CGGTTCACAG AGGTCAGGGA GTTTGCCATT GTTCCCCTGC ATGCGGCCCC GGGGGACGCA
     1201 GTAGCCGAGA TCGACGCTCT CTATGACGTC TACCTGGATG TCCAAGAGAA ATGGGGCTTG
     1261 GAGGACGTCA TGTTGATGGG CGACTTCAAT GCGGGCTGCA GCTATGTGAG ACCCTCCCAG
     1321 TGGTCATCCA TCCGCCTGTG GACAAGCCCC ACCTTCCAGT GGCTGATCCC CGACAGCGCT
     1381 GACACCACAG CTACACCCAC GCACTGTGCC TATGACAGGA TCGTGGTTGC AGGGATGCTG
     1441 CTCCGAGGGG CCGTTGTTCC CGACTCGGCT CTTCCCTTTA ACTTCCAGGC TGCCTATGGC
     1501 CTGAGTGACC AACTGGCCCA AGCCATCAGT GACCACTATC CAGTGGAGGT GATGCTGAAG
     1561 GGGGGCGGAC CCAAAAAGAA GCGCAAGGTT TGA
//
```

```
               9          18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


              63          72          81          90          99         108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


             117         126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


             171         180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


             225         234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


             279         288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


             333         342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


             387         396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


             441         450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


             495         504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


             549         558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

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```
          603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

          657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

          711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

          765         774         783         792         801         810
GAA GGG AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   G   S   G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E

          819         828         837         846         855         864
ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R

          873         882         891         900         909         918
TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Y   D   I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G

          927         936         945         954         963         972
AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 K   L   L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V

          981         990         999         1008        1017        1026
AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   E   P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R

          1035        1044        1053        1062        1071        1080
CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P

          1089        1098        1107        1116        1125        1134
TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   G   N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R

          1143        1152        1161        1170        1179        1188
TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   T   E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D

          1197        1206        1215        1224        1233        1242
```

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```
GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   V   A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K

        1251        1260        1269        1278        1287        1296
TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 W   G   L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y

        1305        1314        1323        1332        1341        1350
GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   R   P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q

        1359        1368        1377        1386        1395        1404
TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 W   L   I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y

        1413        1422        1431        1440        1449        1458
GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   R   I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S

        1467        1476        1485        1494        1503        1512
GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q

        1521        1530        1539        1548        1557        1566
GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA CCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   I   S   D   H   Y   P   V   E   V   M   L   K   G   G   G   P   K

        1575        1584
AAG AAG CGC AAG GTT TGA 3'
--- --- --- --- --- ---
 K   K   R   K   V   *
```

FIGURE 7

(A) pAS34

```
LOCUS         PAS34.DNA    2196 bp          2196 bp  2196 bp  DNA    14-AUG-1998
DEFINITION    HUMANISED HMFG1 heavy chain fused to human DNAse construct 34
DEFINITION    Clone 16.4.2 (same as hcdnase1.dna template file)
REFERENCE
  AUTHORS     VERHOEYEN ET AL
  TITLE       CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL     IMMUNOL. (1993):78, 364-370
COMMENT       Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT       The fusion was made using overlapping oligos AS79 and AS80
FEATURES      AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES      Residue 963 is G > T leading to silent mutation in all clones
  SITES       Note
BASE COUNT       501 a     677 c     607 g     411 t
ORIGIN            ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CTCCGGGTAA AGGGAGCGGC GGGCTGAAGA TCGCAGCCTT CAACATCCAG
1441 ACATTTGGGG AGACCAAGAT GTCCAATGCC ACCCTCGTCA GCTACATTGT GCAGATCCTG
1501 AGCCGCTACG ACATCGCCCT GGTCCAGGAG GTCAGAGACA GCCACCTGAC TGCCGTGGGG
1561 AAGCTGCTGG ACAACCTCAA TCAGGACGCA CCAGACACCT ATCACTACGT GGTCAGTGAG
1621 CCACTGGGAC GGAACAGCTA TAAGGAGCGC TACCTGTTCG TGTACAGGCC TGACCAGGTG
1681 TCTGCGGTGG ACAGCTACTA CTACGATGAT GGCTGCGAGC CCTGCGGGAA CGACACCTTC
1741 AACCGAGAGC CAGCCATTGT CAGGTTCTTC TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC
1801 ATTGTTCCCC TGCATGCGGC CCCGGGGGAC GCAGTAGCCG AGATCGACGC TCTCTATGAC
1861 GTCTACCTGG ATGTCCAAGA GAAATGGGGC TTGGAGGACG TCATGTTGAT GGGCGACTTC
1921 AATGCGGGCT GCAGCTATGT GAGACCCTCC CAGTGGTCAT CCATCCGCCT GTGGACAAGC
1981 CCCACCTTCC AGTGGCTGAT CCCCGACAGC GCTGACACCA CAGCTACACC CACGCACTGT
2041 GCCTATGACA GGATCGTGGT TGCAGGGATG CTGCTCCGAG GGCCGTTGT TCCCGACTCG
2101 GCTCTTCCCT TTAACTTCCA GGCTGCCTAT GGCCTGAGTG ACCAACTGGC CCAAGCCATC
2161 AGTGACCACT ATCCAGTGGA GGTGATGCTG AAGTGA
//
```

FIGURE 7(B)

```
            9           18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H

            63          72          81          90          99         108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S

           117         126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

           171         180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

           225         234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

           279         288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

           333         342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

           387         396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

           441         450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

           495         504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

           549         558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G

           603         612         621         630         639         648
   CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

           657         666         675         684         693         702
```

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```
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

        765         774         783         792         801         810
GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

        819         828         837         846         855         864
CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

        873         882         891         900         909         918
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

        927         936         945         954         963         972
GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

        981         990         999        1008        1017        1026
GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

       1035        1044        1053        1062        1071        1080
GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

       1089        1098        1107        1116        1125        1134
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

       1143        1152        1161        1170        1179        1188
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

       1197        1206        1215        1224        1233        1242
ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

       1251        1260        1269        1278        1287        1296
CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

       1305        1314        1323        1332        1341        1350
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

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```
          1359            1368            1377            1386            1395            1404
'GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G   K   G̲

          1413            1422            1431            1440            1449            1458
AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S̲   G̲   G̲   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K

          1467            1476            1485            1494            1503            1512
ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D

          1521            1530            1539            1548            1557            1566
ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L

          1575            1584            1593            1602            1611            1620
CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E

          1629            1638            1647            1656            1665            1674
CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D

          1683            1692            1701            1710            1719            1728
CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G

          1737            1746            1755            1764            1773            1782
AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T

          1791            1800            1809            1818            1827            1836
GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V

          1845            1854            1863            1872            1881            1890
GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G

          1899            1908            1917            1926            1935            1944
TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R

          1953            1962            1971            1980            1989            1998
CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L

          2007            2016            2025            2034            2043            2052
ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R
```

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```
              2061          2070          2079          2088          2097          2106
ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L


              2115          2124          2133          2142          2151          2160
CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I


              2169          2178          2187          2196
AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
--- --- --- --- --- --- --- --- --- --- --- ---
 S   D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 8

(A) pAS35

```
LOCUS         PAS35.DNA    2193 bp    2193 bp    DNA              14-AUG-1998
DEFINITION    HUMANISED HMFG1 heavy chain fused to human DNAse construct 35
DEFINITION    Clone 17.12.1 with silent K to K mutation (1398 A > G)
REFERENCE
  AUTHORS     VERHOEYEN ET AL
  TITLE       CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL     IMMUNOL. (1993):78, 364-370
COMMENT       Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT       The fusion was made using overlapping oligos AS81 and AS82
FEATURES      AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES      Residue 963 is G > T leading to silent mutation in all clones
FEATURES      In 17.12.1 residue 1398 is A > G (silent K to K mutation)
  SITES       Note
BASE COUNT       500 a    677 c    606 g    410 t
ORIGIN           ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CTCCGAAgGG GAGCGGCGGG CTGAAGATCG CAGCCTTCAA CATCCAGACA
1441 TTTGGGGAGA CCAAGATGTC CAATGCCACC CTCGTCAGCT ACATTGTGCA GATCCTGAGC
1501 CGCTACGACA TCGCCCTGGT CCAGGAGGTC AGAGACAGCC ACCTGACTGC CGTGGGGAAG
1561 CTGCTGGACA ACCTCAATCA GGACGCACCA GACACCTATC ACTACGTGGT CAGTGAGCCA
1621 CTGGGACGGA ACAGCTATAA GGAGCGCTAC CTGTTCGTGT ACAGGCCTGA CCAGGTGTCT
1681 GCGGTGGACA GCTACTACTA CGATGATGGC TGCGAGCCCT GCGGGAACGA CACCTTCAAC
1741 CGAGAGCCAG CCATTGTCAG GTTCTTCTCC CGGTTCACAG AGGTCAGGGA GTTTGCCATT
1801 GTTCCCCTGC ATGCGGCCCC GGGGGACGCA GTAGCCGAGA TCGACGCTCT CTATGACGTC
1861 TACCTGGATG TCCAAGAGAA ATGGGGCTTG GAGGACGTCA TGTTGATGGG CGACTTCAAT
1921 GCGGGCTGCA GCTATGTGAG ACCCTCCCAG TGGTCATCCA TCCGCCTGTG GACAAGCCCC
1981 ACCTTCCAGT GGCTGATCCC CGACAGCGCT GACACCACAG CTACACCCAC GCACTGTGCC
2041 TATGACAGGA TCGTGGTTGC AGGGATGCTG CTCCGAGGGG CCGTTGTTCC CGACTCGGCT
2101 CTTCCCTTTA ACTTCCAGGC TGCCTATGGC CTGAGTGACC AACTGGCCCA AGCCATCAGT
2161 GACCACTATC AGTGGAGGT GATGCTGAAG TGA
//
```

```
              9          18          27          36          45          54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H
     =

              63          72          81          90          99         108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S
    ===

             117         126         135         144         153         162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

             171         180         189         198         207         216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

             225         234         243         252         261         270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

             279         288         297         306         315         324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

             333         342         351         360         369         378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

             387         396         405         414         423         432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

             441         450         459         468         477         486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

             495         504         513         522         531         540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

             549         558         567         576         585         594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G

             603         612         621         630         639         648
    CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

             657         666         675         684         693         702
```

```
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

        765         774         783         792         801         810
GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

        819         828         837         846         855         864
CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

        873         882         891         900         909         918
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

        927         936         945         954         963         972
GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

        981         990         999        1008        1017        1026
GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

       1035        1044        1053        1062        1071        1080
GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

       1089        1098        1107        1116        1125        1134
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

       1143        1152        1161        1170        1179        1188
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

       1197        1206        1215        1224        1233        1242
ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

       1251        1260        1269        1278        1287        1296
CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

       1305        1314        1323        1332        1341        1350
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

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```
        1359            1368            1377            1386            1395            1404
GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG AAG GGG AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   K   G   S


        1413            1422            1431            1440            1449            1458
GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG ATG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K   M


        1467            1476            1485            1494            1503            1512
TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D   I


        1521            1530            1539            1548            1557            1566
GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L   L


        1575            1584            1593            1602            1611            1620
GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG CCA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E   P


        1629            1638            1647            1656            1665            1674
CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D   Q


        1683            1692            1701            1710            1719            1728
GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG AAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G   N


        1737            1746            1755            1764            1773            1782
GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T   E


        1791            1800            1809            1818            1827            1836
GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA GCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V   A


        1845            1854            1863            1872            1881            1890
GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC TTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G   L


        1899            1908            1917            1926            1935            1944
GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R   P


        1953            1962            1971            1980            1989            1998
TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L   I


        2007            2016            2025            2034            2043            2052
CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R   I
```

```
         2061        2070        2079        2088        2097        2106
GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L   P

         2115        2124        2133        2142        2151        2160
TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC AGT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I   S

         2169        2178        2187
GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
--- --- --- --- --- --- --- --- --- --- ---
 D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 9

(A) pAS36

```
LOCUS          PAS36.DNA    2190 bp  2190 bp     DNA                  14-AUG-1998
DEFINITION     HUMANISED HMFG1 heavy chain fused to human DNAse - construct 36
DEFINITION     Clone 18.24.1 with residue 1392 T > C
REFERENCE
  AUTHORS      VERHOEYEN ET AL
  TITLE        CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL      IMMUNOL. (1993):78, 364-370
COMMENT        Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT        The fusion was made using overlapping oligos AS83 and AS84
FEATURES       AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES       Residue 963 is G > T leading to silent mutation in all clones
FEATURES       Residue 1392 T > C silent S to S mutation
  SITES        Note
BASE COUNT       498 a    678 c    605 g    409 t
ORIGIN            ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CCCCGGGGAG CGGCGGGCTG AAGATCGCAG CCTTCAACAT CCAGACATTT
1441 GGGGAGACCA AGATGTCCAA TGCCACCCTC GTCAGCTACA TTGTGCAGAT CCTGAGCCGC
1501 TACGACATCG CCCTGGTCCA GGAGGTCAGA GACAGCCACC TGACTGCCGT GGGGAAGCTG
1561 CTGGACAACC TCAATCAGGA CGCACCAGAC ACCTATCACT ACGTGGTCAG TGAGCCACTG
1621 GGACGGAACA GCTATAAGGA GCGCTACCTG TTCGTGTACA GGCCTGACCA GGTGTCTGCG
1681 GTGGACAGCT ACTACTACGA TGATGGCTGC GAGCCCTGCG GGAACGACAC CTTCAACCGA
1741 GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG TTCACAGAGG TCAGGGAGTT TGCCATTGTT
1801 CCCCTGCATG CGGCCCCGGG GGACGCAGTA GCCGAGATCG ACGCTCTCTA TGACGTCTAC
1861 CTGGATGTCC AAGAGAAATG GGGCTTGGAG GACGTCATGT TGATGGGCGA CTTCAATGCG
1921 GGCTGCAGCT ATGTGAGACC CTCCCAGTGG TCATCCATCC GCCTGTGGAC AAGCCCCACC
1981 TTCCAGTGGC TGATCCCCGA CAGCGCTGAC ACCACAGCTA CACCCACGCA CTGTGCCTAT
2041 GACAGGATCG TGGTTGCAGG GATGCTGCTC CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT
2101 CCCTTTAACT TCCAGGCTGC CTATGGCCTG AGTGACCAAC TGGCCCAAGC CATCAGTGAC
2161 CACTATCCAG TGGAGGTGAT GCTGAAGTGA
//
```

```
                9              18              27              36              45              54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H
    ─────────────────────────────────────────────────────────────────────

                63             72              81              90              99             108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S
    ───

               117            126             135             144             153             162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

               171            180             189             198             207             216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

               225            234             243             252             261             270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

               279            288             297             306             315             324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

               333            342             351             360             369             378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

               387            396             405             414             423             432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

               441            450             459             468             477             486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

               495            504             513             522             531             540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

               549            558             567             576             585             594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G

               603            612             621             630             639             648
    CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

               657            666             675             684             693             702
```

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```
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

         711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

         765         774         783         792         801         810
GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

         819         828         837         846         855         864
CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

         873         882         891         900         909         918
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

         927         936         945         954         963         972
GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

         981         990         999        1008        1017        1026
GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

        1035        1044        1053        1062        1071        1080
GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

        1089        1098        1107        1116        1125        1134
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

        1143        1152        1161        1170        1179        1188
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

        1197        1206        1215        1224        1233        1242
ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

        1251        1260        1269        1278        1287        1296
CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

        1305        1314        1323        1332        1341        1350
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

```
          1359          1368          1377          1386          1395          1404
GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCC CCG GGG AGC GGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G   S   G
                                                                ‾‾‾‾‾‾‾‾‾‾‾
          1413          1422          1431          1440          1449          1458
GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG ATG TCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K   M   S
‾‾‾
          1467          1476          1485          1494          1503          1512
AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC ATC GCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D   I   A

          1521          1530          1539          1548          1557          1566
CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG CTG GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L   L   D

          1575          1584          1593          1602          1611          1620
AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG CCA CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E   P   L

          1629          1638          1647          1656          1665          1674
GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC CAG GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D   Q   V

          1683          1692          1701          1710          1719          1728
TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG AAC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G   N   D

          1737          1746          1755          1764          1773          1782
ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA GAG GTC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T   E   V

          1791          1800          1809          1818          1827          1836
AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA GCC GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V   A   E

          1845          1854          1863          1872          1881          1890
ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC TTG GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G   L   E

          1899          1908          1917          1926          1935          1944
GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA CCC TCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R   P   S

          1953          1962          1971          1980          1989          1998
CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG ATC CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L   I   P

          2007          2016          2025          2034          2043          2052
GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG ATC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R   I   V
```

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```
        2061          2070          2079          2088          2097          2106
.GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT CCC TTT
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L   P   F

        2115          2124          2133          2142          2151          2160
AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC AGT GAC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I   S   D

        2169          2178          2187
CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
 --- --- --- --- --- --- --- --- --- ---
  H   Y   P   V   E   V   M   L   K   *
```

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FIGURE 10

(A) pAS37

```
LOCUS         PAS37.DNA    2226 bp        2196 bp  2196 bp DNA       14-AUG-1998
DEFINITION    HUMANISED HMFG1 heavy chain fused to human DNAse construct 37
DEFINITION    Clone 16.4.2 (same as hcdnase1.dna template file) plus NLS
REFERENCE
  AUTHORS     VERHOEYEN ET AL
  TITLE       CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL     IMMUNOL. (1993):78, 364-370
COMMENT       Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT       The fusion was made using overlapping oligos AS79 and AS80
FEATURES      AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES      Residue 963 is G > T leading to silent mutation in all clones
  SITES       Note
BASE COUNT      511 a    683 c    619 g    413 t
ORIGIN          ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CTCCGGGTAA AGGGAGCGGC GGGCTGAAGA TCGCAGCCTT CAACATCCAG
1441 ACATTTGGGG AGACCAAGAT GTCCAATGCC ACCCTCGTCA GCTACATTGT GCAGATCCTG
1501 AGCCGCTACG ACATCGCCCT GGTCCAGGAG GTCAGAGACA GCCACCTGAC TGCCGTGGGG
1561 AAGCTGCTGG ACAACCTCAA TCAGGACGCA CCAGACACCT ATCACTACGT GGTCAGTGAG
1621 CCACTGGGAC GGAACAGCTA TAAGGAGCGC TACCTGTTCG TGTACAGGCC TGACCAGGTG
1681 TCTGCGGTGG ACAGCTACTA CTACGATGAT GGCTGCGAGC CTGCGGGAA CGACACCTTC
1741 AACCGAGAGC CAGCCATTGT CAGGTTCTTC TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC
1801 ATTGTTCCCC TGCATGCGGC CCCGGGGGAC GCAGTAGCCG AGATCGACGC TCTCTATGAC
1861 GTCTACCTGG ATGTCCAAGA GAAATGGGGC TTGGAGGACG TCATGTTGAT GGGCGACTTC
1921 AATGCGGGCT GCAGCTATGT GAGACCCTCC CAGTGGTCAT CCATCCGCCT GTGGACAAGC
1981 CCCACCTTCC AGTGGCTGAT CCCCGACAGC GCTGACACCA CAGCTACACC CACGCACTGT
2041 GCCTATGACA GGATCGTGGT TGCAGGGATG CTGCTCCGAG GGGCCGTTGT TCCCGACTCG
2101 GCTCTTCCCT TTAACTTCCA GGCTGCCTAT GGCCTGAGTG ACCAACTGGC CCAAGCCATC
2161 AGTGACCACT ATCCAGTGGA GGTGATGCTG AAGGGGGGCG ACCCAAAAA GAAGCGCAAG
2221 GTTTGA
```

//

$\llcorner$→ NLS

FIGURE 10 (B)

```
              9           18          27          36          45          54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H
    _____

             63          72          81          90          99         108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S
    ___

            117         126         135         144         153         162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

            171         180         189         198         207         216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

            225         234         243         252         261         270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

            279         288        ·297         306         315         324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

            333         342         351         360         369         378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

            387         396         405         414         423         432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

            441         450         459         468         477         486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

            495         504         513         522         531         540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

            549         558         567         576         585         594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G

            603         612         621         630         639         648
    CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --
     L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

            657         666         675         684         693         702
```

```
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

     711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

     765         774         783         792         801         810
GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

     819         828         837         846         855         864
CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

     873         882         891         900         909         918
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

     927         936         945         954         963         972
GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

     981         990         999        1008        1017        1026
GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

    1035        1044        1053        1062        1071        1080
GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

    1089        1098        1107        1116        1125        1134
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

    1143        1152        1161        1170        1179        1188
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

    1197        1206        1215        1224        1233        1242
ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

    1251        1260        1269        1278        1287        1296
CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

    1305        1314        1323        1332        1341        1350
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

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```
        1359        1368        1377        1386        1395        1404
.GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA GGG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G   K   G


        1413        1422        1431        1440        1449        1458
AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  S   G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K


        1467        1476        1485        1494        1503        1512
ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D


        1521        1530        1539        1548        1557        1566
ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L


        1575        1584        1593        1602        1611        1620
CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E


        1629        1638        1647        1656        1665        1674
CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D


        1683        1692        1701        1710        1719        1728
CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G


        1737        1746        1755        1764        1773        1782
AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T


        1791        1800        1809        1818        1827        1836
GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V


        1845        1854        1863        1872        1881        1890
GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G


        1899        1908        1917        1926        1935        1944
TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R


        1953        1962        1971        1980        1989        1998
CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L


        2007        2016        2025        2034        2043        2052
ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R
```

```
         2061            2070              2079              2088              2097              2106
ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L


         2115            2124              2133              2142              2151              2160
CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I


         2169            2178              2187              2196              2205              2214
AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA CCC AAA AAG AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   D   H   Y   P   V   E   V   M   L   K   G   G   G   P   K   K   K
                                                   ‗‗‗‗‗‗‗‗‗‗‗‗‗‗‗‗‗‗‗


         2223
CGC AAG GTT TGA 3'
--- --- --- ---
 R   K   V   *
‗‗‗‗‗‗‗‗‗‗‗‗‗
```

FIGURE 11

(A) pAS38

```
LOCUS       PAS38.DNA      2223 bp     2193 bp     DNA              14-AUG-1998
DEFINITION  HUMANISED HMFG1 heavy chain fused to human DNAse construct 38
DEFINITION  Clone 17.12.1 with silent K to K mutation (1398 A > G)+NLS
REFERENCE
  AUTHORS   VERHOEYEN ET AL
  TITLE     CONSTRUCTION OF RESHAPED HMFG1 etc
  JOURNAL   IMMUNOL. (1993):78, 364-370
COMMENT     Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT     The fusion was made using overlapping oligos AS81 and AS82
FEATURES    AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES    Residue 963 is G > T leading to silent mutation in all clones
FEATURES    In 17.12.1 residue 1398 is A > G (silent K to K mutation)
  SITES     Note
BASE COUNT      510 a     683 c     618 g     412 t
ORIGIN          ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CTCCGAAgGG GAGCGGCGGG CTGAAGATCG CAGCCTTCAA CATCCAGACA
1441 TTTGGGGAGA CCAAGATGTC CAATGCCACC CTCGTCAGCT ACATTGTGCA GATCCTGAGC
1501 CGCTACGACA TCGCCCTGGT CCAGGAGGTC AGAGACAGCC ACCTGACTGC CGTGGGGAAG
1561 CTGCTGGACA ACCTCAATCA GGACGCACCA GACACCTATC ACTACGTGGT CAGTGAGCCA
1621 CTGGGACGGA ACAGCTATAA GGAGCGCTAC CTGTTCGTGT ACAGGCCTGA CCAGGTGTCT
1681 GCGGTGGACA GCTACTACTA CGATGATGGC TGCGAGCCCT GCGGGAACGA CACCTTCAAC
1741 CGAGAGCCAG CCATTGTCAG GTTCTTCTCC CGGTTCACAG AGGTCAGGGA GTTTGCCATT
1801 GTTCCCCTGC ATGCGGCCCC GGGGGACGCA GTAGCCGAGA TCGACGCTCT CTATGACGTC
1861 TACCTGGATG TCCAAGAGAA ATGGGGCTTG GAGGACGTCA TGTTGATGGG CGACTTCAAT
1921 GCGGGCTGCA GCTATGTGAG ACCCTCCCAG TGGTCATCCA TCCGCCTGTG GACAAGCCCC
1981 ACCTTCCAGT GGCTGATCCC CGACAGCGCT GACACCACAG CTACACCCAC GCACTGTGCC
2041 TATGACAGGA TCGTGGTTGC AGGGATGCTG CTCCGAGGGG CCGTTGTTCC CGACTCGGCT
2101 CTTCCCTTTA ACTTCCAGGC TGCCTATGGC CTGAGTGACC AACTGGCCCA AGCCATCAGT
2161 GACCACTATC AGTGGAGGT GATGCTGAAG GGGGGCGGAC CCAAAAAGAA GCGCAAGGTT
2221 TGA
```

//

L₃NLS

FICURE 11 (B)

```
           9          18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H

           63          72          81          90          99         108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S

          117         126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

          171         180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

          225         234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

          279         288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

          333         342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

          387         396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

          441         450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

          495         504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

          549         558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G

          603         612         621         630         639         648
   CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

          657         666         675         684         693         702
```

```
        ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

             711         720         729         738         747         756
        GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

             765         774         783         792         801         810
        GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

             819         828         837         846         855         864
        CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

             873         882         891         900         909         918
        GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

             927         936         945         954         963         972
        GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

             981         990         999        1008        1017        1026
        GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

            1035        1044        1053        1062        1071        1080
        GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

            1089        1098        1107        1116        1125        1134
        GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

            1143        1152        1161        1170        1179        1188
        ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

            1197        1206        1215        1224        1233        1242
        ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- - - - ---
         I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

            1251        1260        1269        1278        1287        1296
        CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

            1305        1314        1323        1332        1341        1350
        GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
         D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

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```
              1359          1368          1377          1386          1395          1404
. GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG AAG GGG AGC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   K   G   S

              1413          1422          1431          1440          1449          1458
  GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG ATG
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K   M

              1467          1476          1485          1494          1503          1512
  TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC ATC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D   I

              1521          1530          1539          1548          1557          1566
  GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG CTG
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L   L

              1575          1584          1593          1602          1611          1620
  GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG CCA
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E   P

              1629          1638          1647          1656          1665          1674
  CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC CAG
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D   Q

              1683          1692          1701          1710          1719          1728
  GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG AAC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G   N

              1737          1746          1755          1764          1773          1782
  GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA GAG
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T   E

              1791          1800          1809          1818          1827          1836
  GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA GCC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V   A

              1845          1854          1863          1872          1881          1890
  GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC TTG
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G   L

              1899          1908          1917          1926          1935          1944
  GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA CCC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R   P

              1953          1962          1971          1980          1989          1998
  TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG ATC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L   I

              2007          2016          2025          2034          2043          2052
  CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG ATC
  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R   I
```

```
         2061            2070            2079            2088            2097            2106
GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L   P

         2115            2124            2133            2142            2151            2160
TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC AGT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I   S

         2169            2178            2187            2196            2205            2214
GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA CCC AAA AAG AAG CGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   H   Y   P   V   E   V   M   L   K   G   G   G   P   K   K   K   R
                                           =====================================

         2223
AAG GTT TGA 3'
--- --- ---
 K   V   *
=============
```

FIGURE 12

(A) pAS39

```
LOCUS          PAS39.DNA    2220 bp   2190 bp    DNA                 14-AUG-1998
DEFINITION     HUMANISED HMFG1 heavy chain fused to human DNAse - construct 39
DEFINITION     Clone 18.24.1 with residue 1392 T > C +NLS
REFERENCE
   AUTHORS     VERHOEYEN ET AL
   TITLE       CONSTRUCTION OF RESHAPED HMFG1 etc
   JOURNAL     IMMUNOL. (1993):78, 364-370
COMMENT        Human DNAse sequence is modified as a result of oligo assembly
(mhdnase.dna)
COMMENT        The fusion was made using overlapping oligos AS83 and AS84
FEATURES       AA RESIDUE 235 HAS NOT BEEN CHANGED TO KABAT (I.E. V TO A)
FEATURES       Residue 963 is G > T leading to silent mutation in all clones
FEATURES       Residue 1392 T > C silent S to S mutation
   SITES       Note
BASE COUNT        508 a     684 c     617 g      411 t
ORIGIN            ?
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCCTCC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAGTC
 781 TTCCTCTTCC CCCCAAAACC CAAGGACACC CTCATGATCT CCCGGACCCC TGAGGTCACA
 841 TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG GTACGTGGAC
 901 GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC
 961 CGTGTGGTCA GCGTCCTCAC CGTCCTGCAC CAGGACTGGC TGAATGGCAA GGAGTACAAG
1021 TGCAAGGTCT CCAACAAAGC CCTCCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA
1081 GGGCAGCCCC GAGAACCACA GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG
1141 AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1201 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT GCTGGACTCC
1261 GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA AGAGCAGGTG GCAGCAGGGG
1321 AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC
1381 CTCTCCCTGT CcCCGGGGAG CGGCGGGCTG AAGATCGCAG CCTTCAACAT CCAGACATTT
1441 GGGGAGACCA AGATGTCCAA TGCCACCCTC GTCAGCTACA TTGTGCAGAT CCTGAGCCGC
1501 TACGACATCG CCCTGGTCCA GGAGGTCAGA GACAGCCACC TGACTGCCGT GGGGAAGCTG
1561 CTGGACAACC TCAATCAGGA CGCACCAGAC ACCTATCACT ACGTGGTCAG TGAGCCACTG
1621 GGACGGAACA GCTATAAGGA GCGCTACCTG TTCGTGTACA GGCCTGACCA GGTGTCTGCG
1681 GTGGACAGCT ACTACTACGA TGATGGCTGC GAGCCCTGCG GAACGACAC CTTCAACCGA
1741 GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG TTCACAGAGG TCAGGGAGTT TGCCATTGTT
1801 CCCCTGCATG CGGCCCCGGG GGACGCAGTA GCCGAGATCG ACGCTCTCTA TGACGTCTAC
1861 CTGGATGTCC AAGAGAAATG GGGCTTGGAG GACGTCATGT TGATGGGCGA CTTCAATGCG
1921 GGCTGCAGCT ATGTGAGACC CTCCCAGTGG TCATCCATCC GCCTGTGGAC AAGCCCCACC
1981 TTCCAGTGGC TGATCCCCGA CAGCGCTGAC ACCACAGCTA CACCCACGCA CTGTGCCTAT
2041 GACAGGATCG TGGTTGCAGG GATGCTGCTC CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT
2101 CCCTTTAACT TCCAGGCTGC CTATGGCCTG AGTGACCAAC TGGCCCAAGC CATCAGTGAC
2161 CACTATCCAG TGGAGGTGAT GCTGAAGGGG GGCGGACCCA AAAAGAAGCG CAAGGTTTGA
```

//

```
              9             18            27            36            45            54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H
```

```
              63            72            81            90            99           108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S
```

```
             117           126           135           144           153           162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E
```

```
             171           180           189           198           207           216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P
```

```
             225           234           243           252           261           270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T
```

```
             279           288           297           306           315           324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E
```

```
             333           342           351           360           369           378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y
```

```
             387           396           405           414           423           432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S
```

```
             441           450           459           468           477           486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L
```

```
             495           504           513           522           531           540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S
```

```
             549           558           567           576           585           594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

```
             603           612           621           630           639           648
   CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q
```

```
      657           666           675           684           693           702
```

```
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

        765         774         783         792         801         810
GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   L   L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T

        819         828         837         846         855         864
CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S   H

        873         882         891         900         909         918
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N

        927         936         945         954         963         972
GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S

        981         990         999        1008        1017        1026
GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K

       1035        1044        1053        1062        1071        1080
GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   S   N   K   A   L   P   A   P   I   E   K   T   I   S   K   A   K

       1089        1098        1107        1116        1125        1134
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   R   D   E   L

       1143        1152        1161        1170        1179        1188
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D

       1197        1206        1215        1224        1233        1242
ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T

       1251        1260        1269        1278        1287        1296
CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   P   V   L   D   S   D   G   S   F   F   L   Y   S   K   L   T   V

       1305        1314        1323        1332        1341        1350
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V   M   H   E
```

```
        1359            1368            1377            1386            1395            1404
·GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCC CCG GGG AGC GGC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G   S   G
                                                                ___ ___ ___

        1413            1422            1431            1440            1449            1458
 GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG ATG TCC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K   M   S
 ___

        1467            1476            1485            1494            1503            1512
 AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC ATC GCC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D   I   A

        1521            1530            1539            1548            1557            1566
 CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG CTG GAC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L   L   D

        1575            1584            1593            1602            1611            1620
 AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG CCA CTG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E   P   L

        1629            1638            1647            1656            1665            1674
 GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC CAG GTG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D   Q   V

        1683            1692            1701            1710            1719            1728
 TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG AAC GAC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G   N   D

        1737            1746            1755            1764            1773            1782
 ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA GAG GTC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T   E   V

        1791            1800            1809            1818            1827            1836
 AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA GCC GAG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V   A   E

        1845            1854            1863            1872            1881            1890
 ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC TTG GAG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G   L   E

        1899            1908            1917            1926            1935            1944
 GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA CCC TCC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R   P   S

        1953            1962            1971            1980            1989            1998
 CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG ATC CCC
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L   I   P

        2007            2016            2025            2034            2043            2052
 GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG ATC GTG
 --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
  D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R   I   V
```

```
        2061          2070          2079          2088          2097          2106
GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT CCC TTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L   P   F

        2115          2124          2133          2142          2151          2160
AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC AGT GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I   S   D

        2169          2178          2187          2196          2205          2214
CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA CCC AAA AAG AAG CGC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 H   Y   P   V   E   V   M   L   K   G   G   G   P   K   K   K   R   K
                                       ‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾

GTT TGA 3'
--- ---
 V   *
‾‾‾
```

FIGURE 13

(A) pAS101

```
LOCUS         PAS101.DNA    1548 bp    mRNA           PRI        06-MAR-1995
DEFINITION    Humanised HMFG1 Fab'2 fused to human DNase I (pAS101)
ACCESSION
NID
KEYWORDS      DNase I.
SOURCE        DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
   ORGANISM   Homo sapiens
              Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
              Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
   AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
   TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
              sputum
   JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
   MEDLINE    91067672
BASE COUNT       343 a     467 c     430 g      308 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAG GCGGGCTGAA GATCGCAGCC
 781 TTCAACATCC AGACATTTGG GGAGACCAAG ATGTCCAATG CCACCCTCGT CAGCTACATT
 841 GTGCAGATCC TGAGCCGCTA CGACATCGCC CTGGTCCAGG AGGTCAGAGA CAGCCACCTG
 901 ACTGCCGTGG GGAAGCTGCT GGACAACCTC AATCAGGACG CACCAGACAC CTATCACTAC
 961 GTGGTCAGTG AGCCACTGGG ACGGAACAGC TATAAGGAGC GCTACCTGTT CGTGTACAGG
1021 CCTGACCAGG TGTCTGCGGT GGACAGCTAC TACTACGATG ATGGCTGCGA GCCCTGCGGG
1081 AACGACACCT TCAACCGAGA GCCAGCCATT GTCAGGTTCT TCTCCCGGTT CACAGAGGTC
1141 AGGGAGTTTG CCATTGTTCC CCTGCATGCG GCCCCGGGGG ACGCAGTAGC CGAGATCGAC
1201 GCTCTCTATG ACGTCTACCT GGATGTCCAA GAGAAATGGG GCTTGGAGGA CGTCATGTTG
1261 ATGGGCGACT TCAATGCGGG CTGCAGCTAT GTGAGACCCT CCCAGTGGTC ATCCATCCGC
1321 CTGTGGACAA GCCCCACCTT CCAGTGGCTG ATCCCCGACA GCGCTGACAC CACAGCTACA
1381 CCCACGCACT GTGCCTATGA CAGGATCGTG GTTGCAGGGA TGCTGCTCCG AGGGGCCGTT
1441 GTTCCCGACT CGGCTCTTCC CTTTAACTTC CAGGCTGCCT ATGGCCTGAG TGACCAACTG
1501 GCCCAAGCCA TCAGTGACCA CTATCCAGTG GAGGTGATGC TGAAGTGA
//
```

Figure 13 (B)

```
LOCUS       FDDNASE101   1548 BP SS-DNA          SYN        25-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES                 Location/Qualifiers
     frag                join(1..>720,<781..1548)
                         /note="1 to 1548 of PAS101.dna [Split]"
     frag                721..780
                         /note="1 to 60 of 101/105linker"
     frag                join(721..>735,<736..>759,<760..>780)
                         /note="1 to 80 of 102linker [Split]"
BASE COUNT      343 A      465 C      431 G      309 T        0 OTHER
ORIGIN      -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGTCC ACCGTGTCCA GCACCAGAGG GCGGGCTGAA GATCGCAGCC
      781 TTCAACATCC AGACATTTGG GGAGACCAAG ATGTCCAATG CCACCCTCGT CAGCTACATT
      841 GTGCAGATCC TGAGCCGCTA CGACATCGCC CTGGTCCAGG AGGTCAGAGA CAGCCACCTG
      901 ACTGCCGTGG GGAAGCTGCT GGACAACCTC AATCAGGACG CACCAGACAC CTATCACTAC
      961 GTGGTCAGTG AGCCACTGGG ACGGAACAGC TATAAGGAGC GCTACCTGTT CGTGTACAGG
     1021 CCTGACCAGG TGTCTGCGGT GGACAGCTAC TACTACGATG ATGGCTGCGA GCCCTGCGGG
     1081 AACGACACCT TCAACCGAGA GCCAGCCATT GTCAGGTTCT TCTCCCGGTT CACAGAGGTC
     1141 AGGGAGTTTG CCATTGTTCC CCTGCATGCG GCCCCGGGGG ACGCAGTAGC CGAGATCGAC
     1201 GCTCTCTATG ACGTCTACCT GGATGTCCAA GAGAAATGGG GCTTGGAGGA CGTCATGTTG
     1261 ATGGGCGACT TCAATGCGGG CTGCAGCTAT GTGAGACCCT CCCAGTGGTC ATCCATCCGC
     1321 CTGTGGACAA GCCCCACCTT CCAGTGGCTG ATCCCCGACA GCGCTGACAC CACAGCTACA
     1381 CCCACGCACT GTGCCTATGA CAGGATCGTG GTTGCAGGGA TGCTGCTCCG AGGGGCCGTT
     1441 GTTCCCGACT CGGCTCTTCC CTTTAACTTC CAGGCTGCCT ATGGCCTGAG TGACCAACTG
     1501 GCCCAAGCCA TCAGTGACCA CTATCCAGTG GAGGTGATGC TGAAGTGA
//
```

```
LOCUS       FDDNASE101   1557 BP SS-DNA            SYN        29-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES               Location/Qualifiers
     frag              10..1557
                       /note="1 to 1548 of FdDNase101correct"
     frag              join(10..>729,<790..1557)
                       /note="1 to 1548 of PAS101.dna [Split]"
     frag              730..789
                       /note="1 to 60 of 101/105linker"
     frag              join(730..>744,<745..>768,<769..>789)
                       /note="1 to 80 of 102linker [Split]"
BASE COUNT       344 A     471 C     433 G     309 T       0 OTHER
ORIGIN      -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT ACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGTCCA CCGTGTCCAG CACCAGAGGG CGGGCTGAAG
      781 ATCGCAGCCT TCAACATCCA GACATTTGGG GAGACCAAGA TGTCCAATGC CACCCTCGTC
      841 AGCTACATTG TGCAGATCCT GAGCCGCTAC GACATCGCCC TGGTCCAGGA GGTCAGAGAC
      901 AGCCACCTGA CTGCCGTGGG GAAGCTGCTG GACAACCTCA ATCAGGACGC ACCAGACACC
      961 TATCACTACG TGGTCAGTGA GCCACTGGGA CGGAACAGCT ATAAGGAGCG CTACCTGTTC
     1021 GTGTACAGGC CTGACCAGGT GTCTGCGGTG GACAGCTACT ACTACGATGA TGGCTGCGAG
     1081 CCCTGCGGGA ACGACACCTT CAACCGAGAG CCAGCCATTG TCAGGTTCTT CTCCCGGTTC
     1141 ACAGAGGTCA GGGAGTTTGC CATTGTTCCC CTGCATGCGG CCCCGGGGGA CGCAGTAGCC
     1201 GAGATCGACG CTCTCTATGA CGTCTACCTG GATGTCCAAG AGAAATGGGG CTTGGAGGAC
     1261 GTCATGTTGA TGGGCGACTT CAATGCGGGC TGCAGCTATG TGAGACCCTC CCAGTGGTCA
     1321 TCCATCCGCC TGTGGACAAG CCCCACCTTC CAGTGGCTGA TCCCCGACAG CGCTGACACC
     1381 ACAGCTACAC CCACGCACTG TGCCTATGAC AGGATCGTGG TTGCAGGGAT GCTGCTCCGA
     1441 GGGGCCGTTG TTCCCGACTC GGCTCTTCCC TTTAACTTCC AGGCTGCCTA TGGCCTGAGT
     1501 GACCAACTGG CCCAAGCCAT CAGTGACCAC TATCCAGTGG AGGTGATGCT GAAGTGA
//
```

FIGURE 13(D)

```
              9          18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


              63          72          81          90          99         108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


             117         126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


             171         180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


             225         234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


             279         288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


             333         342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


             387         396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


             441         450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


             495         504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


             549         558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

```
        603           612           621           630           639           648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

        657           666           675           684           693           702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711           720           729           738           747           756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P

        765           774           783           792           801           810
GAA GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K

        819           828           837           846           855           864
ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D

        873           882           891           900           909           918
ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L

        927           936           945           954           963           972
CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E

        981           990           999          1008          1017          1026
CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D

       1035          1044          1053          1062          1071          1080
CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G

       1089          1098          1107          1116          1125          1134
AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T

       1143          1152          1161          1170          1179          1188
GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V

       1197          1206          1215          1224          1233          1242
```

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```
GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G

      1251          1260          1269          1278          1287          1296
TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R

      1305          1314          1323          1332          1341          1350
CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L

      1359          1368          1377          1386          1395          1404
ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R

      1413          1422          1431          1440          1449          1458
ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L

      1467          1476          1485          1494          1503          1512
CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I

      1521          1530          1539          1548
AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
--- --- --- --- --- --- --- --- --- --- --- ---
 S   D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 14   (A)   pAS102

```
LOCUS        PAS102.DNA    1566 bp    mRNA            PRI      06-MAR-1995
DEFINITION   Humanised HMFG1 Fab'2 fused to human DNase I (pAS102)
ACCESSION
NID
KEYWORDS     DNase I.
SOURCE       DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna) (see Figure 2)
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
BASE COUNT        345 a     469 c     440 g     312 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCTG TGTGGAGTGC CCACCGTGCC CAGCACCTGA AGGGAGCGGC
 781 GGGCTGAAGA TCGCAGCCTT CAACATCCAG ACATTTGGGG AGACCAAGAT GTCCAATGCC
 841 ACCCTCGTCA GCTACATTGT GCAGATCCTG AGCCGCTACG ACATCGCCCT GGTCCAGGAG
 901 GTCAGAGACA GCCACCTGAC TGCCGTGGGG AAGCTGCTGG ACAACCTCAA TCAGGACGCA
 961 CCAGACACCT ATCACTACGT GGTCAGTGAG CCACTGGGAC GGAACAGCTA TAAGGAGCGC
1021 TACCTGTTCG TGTACAGGCC TGACCAGGTG TCTGCGGTGG ACAGCTACTA CTACGATGAT
1081 GGCTGCGAGC CCTGCGGGAA CGACACCTTC AACCGAGAGC AGCCATTGT CAGGTTCTTC
1141 TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC ATTGTTCCCC TGCATGCGGC CCCGGGGGAC
1201 GCAGTAGCCG AGATCGACGC TCTCTATGAC GTCTACCTGG ATGTCCAAGA GAAATGGGGC
1261 TTGGAGGACG TCATGTTGAT GGGCGACTTC AATGCGGGCT GCAGCTATGT GAGACCCTCC
1321 CAGTGGTCAT CCATCCGCCT GTGGACAAGC CCCACCTTCC AGTGGCTGAT CCCCGACAGC
1381 GCTGACACCA CAGCTACACC CACGCACTGT GCCTATGACA GGATCGTGGT TGCAGGGATG
1441 CTGCTCCGAG GGGCCGTTGT TCCCGACTCG GCTCTTCCCT TTAACTTCCA GGCTGCCTAT
1501 GGCCTGAGTG ACCAACTGGC CCAAGCCATC AGTGACCACT ATCCAGTGGA GGTGATGCTG
1561 AAGTGA
//
```

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Figure 14 (B)

```
 CUS         FDDNASE102    1566 BP SS-DNA                SYN         23-MAR-2001
 FINITION    -
ACCESSION    -
KEYWORDS     -
SOURCE       -
BASE COUNT       345 A      468 C      440 G      313 T       0 OTHER
ORIGIN       -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTCGAGTGT CCACCGTGTC CAGCACCAGA GGGGAGCGGC
      781 GGGCTGAAGA TCGCAGCCTT CAACATCCAG ACATTTGGGG AGACCAAGAT GTCCAATGCC
      841 ACCCTCGTCA GCTACATTGT GCAGATCCTG AGCCGCTACG ACATCGCCCT GGTCCAGGAG
      901 GTCAGAGACA GCCACCTGAC TGCCGTGGGG AAGCTGCTGG ACAACCTCAA TCAGGACGCA
      961 CCAGACACCT ATCACTACGT GGTCAGTGAG CCACTGGGAC GGAACAGCTA TAAGGAGCGC
     1021 TACCTGTTCG TGTACAGGCC TGACCAGGTG TCTGCGGTGG ACAGCTACTA CTACGATGAT
     1081 GGCTGCGAGC CCTGCGGGAA CGACACCTTC AACCGAGAGC CAGCCATTGT CAGGTTCTTC
     1141 TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC ATTGTTCCCC TGCATGCGGC CCCGGGGGAC
     1201 GCAGTAGCCG AGATCGACGC TCTCTATGAC GTCTACCTGG ATGTCCAAGA GAAATGGGGC
     1261 TTGGAGGACG TCATGTTGAT GGGCGACTTC AATGCGGGCT GCAGCTATGT GAGACCCTCC
     1321 CAGTGGTCAT CCATCCGCCT GTGGACAAGC CCCACCTTCC AGTGGCTGAT CCCCGACAGC
     1381 GCTGACACCA CAGCTACACC CACGCACTGT GCCTATGACA GGATCGTGGT TGCAGGGATG
     1441 CTGCTCCGAG GGGCCGTTGT TCCCGACTCG GCTCTTCCCT TTAACTTCCA GGCTGCCTAT
     1501 GGCCTGAGTG ACCAACTGGC CCAAGCCATC AGTGACCACT ATCCAGTGGA GGTGATGCTG
     1561 AAGTGA
//
```

Figure 14 (c)

```
LOCUS        FDDNASE302   1575 BP SS-DNA          SYN        29-AUG-2000
DEFINITION   -
ACCESSION    -                        pAS302
KEYWORDS     -
SOURCE       -
FEATURES                 Location/Qualifiers
      frag               10..1575
                         /note="1 to 1566 of FdDNase102correct"
BASE COUNT       346 A      474 C      442 G      313 T       0 OTHER
ORIGIN       -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT ACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGCTGT GTCGAGTGTC CACCGTGTCC AGCACCAGAG
      781 GGGAGCGGCG GGCTGAAGAT CGCAGCCTTC AACATCCAGA CATTTGGGGA GACCAAGATG
      841 TCCAATGCCA CCCTCGTCAG CTACATTGTG CAGATCCTGA GCCGCTACGA CATCGCCCTG
      901 GTCCAGGAGG TCAGAGACAG CCACCTGACT GCCGTGGGGA AGCTGCTGGA CAACCTCAAT
      961 CAGGACGCAC CAGACACCTA TCACTACGTG GTCAGTGAGC CACTGGGACG GAACAGCTAT
     1021 AAGGAGCGCT ACCTGTTCGT GTACAGGCCT GACCAGGTGT CTGCGGTGGA CAGCTACTAC
     1081 TACGATGATG GCTGCGAGCC CTGCGGGAAC GACACCTTCA ACCGAGAGCC AGCCATTGTC
     1141 AGGTTCTTCT CCCGGTTCAC AGAGGTCAGG GAGTTTGCCA TTGTTCCCCT GCATGCGGCC
     1201 CCGGGGGACG CAGTAGCCGA GATCGACGCT CTCTATGACG TCTACCTGGA TGTCCAAGAG
     1261 AAATGGGGCT TGGAGGACGT CATGTTGATG GGCGACTTCA ATGCGGGCTG CAGCTATGTG
     1321 AGACCCTCCC AGTGGTCATC CATCCGCCTG TGGACAAGCC CCACCTTCCA GTGGCTGATC
     1381 CCCGACAGCG CTGACACCAC AGCTACACCC ACGCACTGTG CCTATGACAG GATCGTGGTT
     1441 GCAGGGATGC TGCTCCGAGG GGCCGTTGTT CCCGACTCGG CTCTTCCCTT TAACTTCCAG
     1501 GCTGCCTATG GCCTGAGTGA CCAACTGGCC CAAGCCATCA GTGACCACTA TCCAGTGGAG
     1561 GTGATGCTGA AGTGA
```

FIGURE 14 (D)

```
            9          18          27          36          45          54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


           63          72          81          90          99         108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


          117         126         135         144         153         162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


          171         180         189         198         207         216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


          225         234         243         252         261         270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- ---' --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


          279         288         297         306         315         324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


          333         342         351         360         369         378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


          387         396         405         414         423         432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


          441         450         459         468         477         486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


          495         504         513         522         531         540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


          549         558         567         576         585         594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

```
          603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q


          657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K


          711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC TGT GTG GAG TGC CCA CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   C   V   E   C   P   P


          765         774         783         792         801         810
TGC CCA GCA CCT GAA GGG AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   P   A   P   E   G   S   G   G   L   K   I   A   A   F   N   I   Q


          819         828         837         846         855         864
ACA TTT GGG GAG ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   F   G   E   T   K   M   S   N   A   T   L   V   S   Y   I   V   Q


          873         882         891         900         909         918
ATC CTG AGC CGC TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   L   S   R   Y   D   I   A   L   V   Q   E   V   R   D   S   H   L


          927         936         945         954         963         972
ACT GCC GTG GGG AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   A   V   G   K   L   L   D   N   L   N   Q   D   A   P   D   T   Y


          981         990         999        1008        1017        1026
CAC TAC GTG GTC AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 H   Y   V   V   S   E   P   L   G   R   N   S   Y   K   E   R   Y   L


         1035        1044        1053        1062        1071        1080
TTC GTG TAC AGG CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   V   Y   R   P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D


         1089        1098        1107        1116        1125        1134
GGC TGC GAG CCC TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   C   E   P   C   G   N   D   T   F   N   R   E   P   A   I   V   R


         1143        1152        1161        1170        1179        1188
TTC TTC TCC CGG TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   F   S   R   F   T   E   V   R   E   F   A   I   V   P   L   H   A


         1197        1206        1215        1224        1233        1242
```

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```
    GCC CCG GGG GAC GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    A   P   G   D   A   V   A   E   I   D   A   L   Y   D   V   Y   L   D

       1251        1260        1269        1278        1287        1296
    GTC CAA GAG AAA TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   Q   E   K   W   G   L   E   D   V   M   L   M   G   D   F   N   A

       1305        1314        1323        1332        1341        1350
    GGC TGC AGC TAT GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   S   Y   V   R   P   S   Q   W   S   S   I   R   L   W   T   S

       1359        1368        1377        1386        1395        1404
    CCC ACC TTC CAG TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    P   T   F   Q   W   L   I   P   D   S   A   D   T   T   A   T   P   T

       1413        1422        1431        1440        1449        1458
    CAC TGT GCC TAT GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    H   C   A   Y   D   R   I   V   V   A   G   M   L   L   R   G   A   V

       1467        1476        1485        1494        1503        1512
    GTT CCC GAC TCG GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   P   D   S   A   L   P   F   N   F   Q   A   A   Y   G   L   S   D

       1521        1530        1539        1548        1557        1566
    CAA CTG GCC CAA GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    Q   L   A   Q   A   I   S   D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 15

(A) pAS103

```
LOCUS          PAS103.DNA    1560 bp    mRNA              PRI        06-MAR-1995
DEFINITION     Humanised HMFG1 Fab'2 fused to human DNase I (pAS103)
ACCESSION
NID
KEYWORDS       DNase I.
SOURCE         DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM     Homo sapiens
               Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
               Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS      Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE        Recombinant human DNase I reduces the viscosity of cystic fibrosis
               sputum
  JOURNAL      Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE      91067672
BASE COUNT       344 a    468 c    436 g    312 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCTG TGTGGAGTGC CCACCGTGCC CAGCACCTGA AGGCGGGCTG
 781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
 841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
 901 GACAGCCACC TGACTGCCGT GGGGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
 961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA GCGCTACCTG
1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
1081 GAGCCCTGCG GAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGTGA
//
```

Figure 15 (B)

```
LOCUS       FDDNASE103    1560 BP SS-DNA           SYN          25-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES              Location/Qualifiers
     frag             join(1..>720,<793..1560)
                      /note="1 to 1560 of PAS103.dna [Split]"
     frag             721..792
                      /note="1 to 72 of 103/107linker"
     frag             join(721..>771,<772..792)
                      /note="1 to 78 of 102linker [Split]"
BASE COUNT      344 A     467 C     436 G     313 T      0 OTHER
ORIGIN       -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTCGAGTGT CCACCGTGTC CAGCACCAGA GGGCGGGCTG
      781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
      841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
      901 GACAGCCACC TGACTGCCGT GGGGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
      961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA GCGCTACCTG
     1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
     1081 GAGCCCTGCG GGAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
     1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
     1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
     1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
     1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
     1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
     1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
     1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGTGA
```

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Figure 15 (C)

```
LOCUS        FDDNASE103    1569 BP SS-DNA          SYN        29-AUG-2000
DEFINITION   -
ACCESSION    -
KEYWORDS     -
SOURCE       -
FEATURES                   Location/Qualifiers
      frag                 10..1569
                           /note="1 to 1560 of FdDNase103correct"
      frag                 join(10..>729,<802..1569)
                           /note="1 to 1560 of PAS103.dna [Split]"
      frag                 730..801
                           /note="1 to 72 of 103/107linker"
      frag                 join(730..>780,<781..801)
                           /note="1 to 78 of 102linker [Split]"
BASE COUNT      345 A     473 C     438 G     313 T        0 OTHER
ORIGIN       -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGCTGT GTCGAGTGTC CACCGTGTCC AGCACCAGAG
      781 GGCGGGCTGA AGATCGCAGC CTTCAACATC CAGACATTTG GGAGACCAA GATGTCCAAT
      841 GCCACCCTCG TCAGCTACAT TGTGCAGATC CTGAGCCGCT ACGACATCGC CCTGGTCCAG
      901 GAGGTCAGAG ACAGCCACCT GACTGCCGTG GGGAAGCTGC TGGACAACCT CAATCAGGAC
      961 GCACCAGACA CCTATCACTA CGTGGTCAGT GAGCCACTGG GACGGAACAG CTATAAGGAG
     1021 CGCTACCTGT TCGTGTACAG GCCTGACCAG GTGTCTGCGG TGGACAGCTA CTACTACGAT
     1081 GATGGCTGCG AGCCCTGCGG GAACGACACC TTCAACCGAG AGCCAGCCAT TGTCAGGTTC
     1141 TTCTCCCGGT TCACAGAGGT CAGGGAGTTT GCCATTGTTC CCTGCATGC GGCCCCGGGG
     1201 GACGCAGTAG CCGAGATCGA CGCTCTCTAT GACGTCTACC TGGATGTCCA AGAGAAATGG
     1261 GGCTTGGAGG ACGTCATGTT GATGGGCGAC TTCAATGCGG GCTGCAGCTA TGTGAGACCC
     1321 TCCCAGTGGT CATCCATCCG CCTGTGGACA AGCCCCACCT TCCAGTGGCT GATCCCCGAC
     1381 AGCGCTGACA CCACAGCTAC ACCCACGCAC TGTGCCTATG ACAGGATCGT GGTTGCAGGG
     1441 ATGCTGCTCC GAGGGGCCGT TGTTCCCGAC TCGGCTCTTC CCTTTAACTT CCAGGCTGCC
     1501 TATGGCCTGA GTGACCAACT GGCCCAAGCC ATCAGTGACC ACTATCCAGT GGAGGTGATG
     1561 CTGAAGTGA
//
```

FIGURE 15 (D)

```
                    9              18             27             36             45             54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


                   63             72             81             90             99            108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


                  117            126            135            144            153            162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


                  171            180            189            198            207            216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


                  225            234            243            252            261            270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


                  279            288            297            306            315            324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


                  333            342            351            360            369            378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


                  387            396            405            414            423            432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


                  441            450            459            468            477            486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


                  495            504            513            522            531            540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


                  549            558            567            576            585            594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

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```
               603         612         621         630         639         648
    CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

               657         666         675         684         693         702
    ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

               711         720         729         738         747         756
    GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC TGT GTG GAG TGC CCA CCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   E   P   K   S   C   D   K   T   H   T   C   C   V   E   C   P   P

               765         774         783         792         801         810
    TGC CCA GCA CCT GAA GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     C   P   A   P   E   G   G   L   K   I   A   A   F   N   I   Q   T   F

               819         828         837         846         855         864
    GGG GAG ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   E   T   K   M   S   N   A   T   L   V   S   Y   I   V   Q   I   L

               873         882         891         900         909         918
    AGC CGC TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   R   Y   D   I   A   L   V   Q   E   V   R   D   S   H   L   T   A

               927         936         945         954         963         972
    GTG GGG AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   G   K   L   L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y

               981         990         999        1008        1017        1026
    GTG GTC AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   V   S   E   P   L   G   R   N   S   Y   K   E   R   Y   L   F   V

              1035        1044        1053        1062        1071        1080
    TAC AGG CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     Y   R   P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C

              1089        1098        1107        1116        1125        1134
    GAG CCC TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     E   P   C   G   N   D   T   F   N   R   E   P   A   I   V   R   F   F

              1143        1152        1161        1170        1179        1188
    TCC CGG TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   R   F   T   E   V   R   E   F   A   I   V   P   L   H   A   A   P

              1197        1206        1215        1224        1233        1242
```

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```
GGG GAC GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   D   A   V   A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q

      1251        1260        1269        1278        1287        1296
GAG AAA TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   K   W   G   L   E   D   V   M   L   M   G   D   F   N   A   G   C

      1305        1314        1323        1332        1341        1350
AGC TAT GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   Y   V   R   P   S   Q   W   S   S   I   R   L   W   T   S   P   T

      1359        1368        1377        1386        1395        1404
TTC CAG TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   Q   W   L   I   P   D   S   A   D   T   T   A   T   P   T   H   C

      1413        1422        1431        1440        1449        1458
GCC TAT GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   Y   D   R   I   V   V   A   G   M   L   L   R   G   A   V   V   P

      1467        1476        1485        1494        1503        1512
GAC TCG GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   S   A   L   P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L

      1521        1530        1539        1548        1557
GCC CAA GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   Q   A   I   S   D   H   Y   P   V   E   V   M   L   K   *
```

FIGURE 16

(A) pAS104

```
LOCUS        PAS104.DNA    1560 bp     mRNA            PRI        06-MAR-1995
DEFINITION   Humanised HMFG1 Fab'2 fused to human DNase I (pAS104)
Position 924 G to A by ggg to gag
Linker GR instead of GG (position 777)
ACCESSION
NID
KEYWORDS     DNase I.
SOURCE       DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
BASE COUNT      346 a     468 c     434 g     312 t
ORIGIN
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTGGAGTGC CCACCGTGCC CAGCACCTGA AGGCAGGCTG
      781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
      841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
      901 GACAGCCACC TGACTGCCGT GGAGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
      961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA CGCGTACCTG
     1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
     1081 GAGCCCTGCG GGAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
     1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
     1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
     1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
     1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
     1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
     1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
     1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGTGA
//
```

Figure 16(B)

LOCUS   FDDNASE104   1560 BP SS-DNA   SYN   25-AUG-2000
DEFINITION -
ACCESSION   -
KEYWORDS   -
SOURCE   -
FEATURES   Location/Qualifiers
     frag   join(1..>720,<793..1560)
                       /note="1 to 1560 of PAS104.dna [Split]"
     frag   721..792
                       /note="1 to 72 of 104linker"
     frag   join(721..>774,<776..792)
                       /note="1 to 72 of 103linker [Split]"
     frag   join(721..>771,<772..>774,<776..792)
                       /note="1 to 78 of 102linker [Split]"
BASE COUNT   346 A   467 C   434 G   313 T   0 OTHER
ORIGIN   -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTCGAGTGT CCACCGTGTC CAGCACCAGA GGGCAGGCTG
      781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
      841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
      901 GACAGCCACC TGACTGCCGT GGAGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
      961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA GCGCTACCTG
     1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
     1081 GAGCCCTGCG GGAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
     1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
     1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
     1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
     1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
     1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
     1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
     1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGTGA
//

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FIGURE 16(C)

```
              9              18             27             36             45             54
5´  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H

             63             72             81             90             99            108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S

            117            126            135            144            153            162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E

            171            180            189            198            207            216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P

            225            234            243            252            261            270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T

            279            288            297            306            315            324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E

            333            342            351            360            369            378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y

            387            396            405            414            423            432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S

            441            450            459            468            477            486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L

            495            504            513            522            531            540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S

            549            558            567            576            585            594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

```
          603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q


          657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K


          711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC TGT GTG GAG TGC CCA CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   C   V   E   C   P   P


          765         774         783         792         801         810
TGC CCA GCA CCT GAA GGC AGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   P   A   P   E   G   R   L   K   I   A   A   F   N   I   Q   T   F


          819         828         837         846         855         864
GGG GAG ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   E   T   K   M   S   N   A   T   L   V   S   Y   I   V   Q   I   L


          873         882         891         900         909         918
AGC CGC TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   R   Y   D   I   A   L   V   Q   E   V   R   D   S   H   L   T   A


          927         936         945         954         963         972
GTG GAG AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   K   L   L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y


          981         990         999         1008        1017        1026
GTG GTC AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   V   S   E   P   L   G   R   N   S   Y   K   E   R   Y   L   F   V


          1035        1044        1053        1062        1071        1080
TAC AGG CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Y   R   P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C


          1089        1098        1107        1116        1125        1134
GAG CCC TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   P   C   G   N   D   T   F   N   R   E   P   A   I   V   R   F   F


          1143        1152        1161        1170        1179        1188
TCC CGG TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   R   F   T   E   V   R   E   F   A   I   V   P   L   H   A   A   P


          1197        1206        1215        1224        1233        1242
```

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```
      GGG GAC GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       G   D   A   V   A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q

         1251        1260        1269        1278        1287        1296
      GAG AAA TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       E   K   W   G   L   E   D   V   M   L   M   G   D   F   N   A   G   C

         1305        1314        1323        1332        1341        1350
      AGC TAT GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       S   Y   V   R   P   S   Q   W   S   S   I   R   L   W   T   S   P   T

         1359        1368        1377        1386        1395        1404
      TTC CAG TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       F   Q   W   L   I   P   D   S   A   D   T   T   A   T   P   T   H   C

         1413        1422        1431        1440        1449        1458
      GCC TAT GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       A   Y   D   R   I   V   V   A   G   M   L   L   R   G   A   V   V   P

         1467        1476        1485        1494        1503        1512
      GAC TCG GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       D   S   A   L   P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L

         1521        1530        1539        1548        1557
      GCC CAA GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG TGA 3'
      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
       A   Q   A   I   S   D   H   Y   P   V   E   V   M   L   K   *
```

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FIGURE 17

(A) pAS105

```
LOCUS        PAS105.DNA   1578 bp      mRNA           PRI        06-MAR-1995
DEFINITION   Humanised HMFG1 Fab'2 fused to human DNase I with SV40 NLS(pAS105)
ACCESSION
NID
KEYWORDS     DNase I.
SOURCE       DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
BASE COUNT      353 a     473 c     442 g     310 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAG GCGGGCTGAA GATCGCAGCC
 781 TTCAACATCC AGACATTTGG GGAGACCAAG ATGTCCAATG CCACCCTCGT CAGCTACATT
 841 GTGCAGATCC TGAGCCGCTA CGACATCGCC CTGGTCCAGG AGGTCAGAGA CAGCCACCTG
 901 ACTGCCGTGG GGAAGCTGCT GGACAACCTC AATCAGGACG CACCAGACAC CTATCACTAC
 961 GTGGTCAGTG AGCCACTGGG ACGGAACAGC TATAAGGAGC GCTACCTGTT CGTGTACAGG
1021 CCTGACCAGG TGTCTGCGGT GGACAGCTAC TACTACGATG ATGGCTGCGA GCCCTGCGGG
1081 AACGACACCT TCAACCGAGA GCCAGCCATT GTCAGGTTCT TCTCCCGGTT CACAGAGGTC
1141 AGGGAGTTTG CCATTGTTCC CCTGCATGCG GCCCCGGGGG ACGCAGTAGC CGAGATCGAC
1201 GCTCTCTATG ACGTCTACCT GGATGTCCAA GAGAAATGGG GCTTGGAGGA CGTCATGTTG
1261 ATGGGCGACT TCAATGCGGG CTGCAGCTAT GTGAGACCCT CCCAGTGGTC ATCCATCCGC
1321 CTGTGGACAA GCCCCACCTT CCAGTGGCTG ATCCCCGACA GCGCTGACAC CACAGCTACA
1381 CCCACGCACT GTGCCTATGA CAGGATCGTG GTTGCAGGGA TGCTGCTCCG AGGGGCCGTT
1441 GTTCCCGACT CGGCTCTTCC CTTTAACTTC CAGGCTGCCT ATGGCCTGAG TGACCAACTG
1501 GCCCAAGCCA TCAGTGACCA CTATCCAGTG GAGGTGATGC TGAAGGGGGG CGGACCCAAA
1561 AAGAAGCGCA AGGTTTGA
// 
```

└→ NLS

Figure 17(B)

```
LOCUS        FDDNASE105    1578 BP SS-DNA              SYN        25-AUG-2000
DEFINITION   -
ACCESSION    -
KEYWORDS     -
SOURCE       -
FEATURES                  Location/Qualifiers
     frag                 join(1..>720,<781..1578)
                          /note="1 to 1578 of PAS105.dna [Split]"
     frag                 721..780
                          /note="1 to 60 of 101/105linker"
     frag                 join(721..>735,<736..>759,<760..>780)
                          /note="1 to 80 of 102linker [Split]"
BASE COUNT       353 A    471 C    443 G    311 T        0 OTHER
ORIGIN       -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGTCC ACCGTGTCCA GCACCAGAGG GCGGGCTGAA GATCGCAGCC
      781 TTCAACATCC AGACATTTGG GGAGACCAAG ATGTCCAATG CCACCCTCGT CAGCTACATT
      841 GTGCAGATCC TGAGCCGCTA CGACATCGCC CTGGTCCAGG AGGTCAGAGA CAGCCACCTG
      901 ACTGCCGTGG GGAAGCTGCT GGACAACCTC AATCAGGACG CACCAGACAC CTATCACTAC
      961 GTGGTCAGTG AGCCACTGGG ACGGAACAGC TATAAGGAGC GCTACCTGTT CGTGTACAGG
     1021 CCTGACCAGG TGTCTGCGGT GGACAGCTAC TACTACGATG ATGGCTGCGA GCCCTGCGGG
     1081 AACGACACCT TCAACCGAGA GCCAGCCATT GTCAGGTTCT TCTCCCGGTT CACAGAGGTC
     1141 AGGGAGTTTG CCATTGTTCC CCTGCATGCG GCCCCGGGGG ACGCAGTAGC CGAGATCGAC
     1201 GCTCTCTATG ACGTCTACCT GGATGTCCAA GAGAAATGGG GCTTGGAGGA CGTCATGTTG
     1261 ATGGGCGACT TCAATGCGGG CTGCAGCTAT GTGAGACCCT CCCAGTGGTC ATCCATCCGC
     1321 CTGTGGACAA GCCCCACCTT CCAGTGGCTG ATCCCGACA GCGCTGACAC CACAGCTACA
     1381 CCCACGCACT GTGCCTATGA CAGGATCGTG GTTGCAGGGA TGCTGCTCCG AGGGGCCGTT
     1441 GTTCCCGACT CGGCTCTTCC CTTTAACTTC CAGGCTGCCT ATGGCCTGAG TGACCAACTG
     1501 GCCCAAGCCA TCAGTGACCA CTATCCAGTG GAGGTGATGC TGAAGGGGGG CGGACCCAAA
     1561 AAGAAGCGCA AGGTTTGA
```

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Figure 17(c)

```
LOCUS        FDDNASE105    1587 BP SS-DNA         SYN        29-AUG-2000
DEFINITION   -
ACCESSION    -
KEYWORDS     -
SOURCE       -
FEATURES               Location/Qualifiers
     frag              10..1587
                       /note="1 to 1578 of FdDNase105correct"
     frag              join(10..>729,<790..1587)
                       /note="1 to 1578 of PAS105.dna [Split]"
     frag              730..789
                       /note="1 to 60 of 101/105linker"
     frag              join(730..>744,<745..>768,<769..>789)
                       /note="1 to 80 of 102linker [Split]"
BASE COUNT       354 A      477 C      445 G      311 T      0 OTHER
ORIGIN       -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGTCCA CCGTGTCCAG CACCAGAGGG CGGGCTGAAG
      781 ATCGCAGCCT TCAACATCCA GACATTTGGG GAGACCAAGA TGTCCAATGC CACCCTCGTC
      841 AGCTACATTG TGCAGATCCT GAGCCGCTAC GACATCGCCC TGGTCCAGGA GGTCAGAGAC
      901 AGCCACCTGA CTGCCGTGGG GAAGCTGCTG GACAACCTCA ATCAGGACGC ACCAGACACC
      961 TATCACTACG TGGTCAGTGA GCCACTGGGA CGGAACAGCT ATAAGGAGCG CTACCTGTTC
     1021 GTGTACAGGC CTGACCAGGT GTCTGCGGTG GACAGCTACT ACTACGATGA TGGCTGCGAG
     1081 CCCTGCGGGA ACGACACCTT CAACCGAGAG CCAGCCATTG TCAGGTTCTT CTCCCGGTTC
     1141 ACAGAGGTCA GGGAGTTTGC CATTGTTCCC CTGCATGCGG CCCCGGGGGA CGCAGTAGCC
     1201 GAGATCGACG CTCTCTATGA CGTCTACCTG GATGTCCAAG AGAAATGGGG CTTGGAGGAC
     1261 GTCATGTTGA TGGGCGACTT CAATGCGGGC TGCAGCTATG TGAGACCCTC CCAGTGGTCA
     1321 TCCATCCGCC TGTGGACAAG CCCCACCTTC CAGTGGCTGA TCCCCGACAG CGCTGACACC
     1381 ACAGCTACAC CCACGCACTG TGCCTATGAC AGGATCGTGG TTGCAGGGAT GCTGCTCCGA
     1441 GGGGCCGTTG TTCCCGACTC GGCTCTTCCC TTTAACTTCC AGGCTGCCTA TGGCCTGAGT
     1501 GACCAACTGG CCCAAGCCAT CAGTGACCAC TATCCAGTGG AGGTGATGCT GAAGGGGGGC
     1561 GGACCCAAAA AGAAGCGCAA GGTTTGA
```

```
                9              18             27             36             45             54
5' ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


                63             72             81             90             99            108
   TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


               117            126            135            144            153            162
   GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


               171            180            189            198            207            216
   TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


               225            234            243            252            261            270
   GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


               279            288            297            306            315            324
   AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


               333            342            351            360            369            378
   GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


               387            396            405            414            423            432
   TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


               441            450            459            468            477            486
   GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


               495            504            513            522            531            540
   GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


               549            558            567            576            585            594
   GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
    G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

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```
        603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q


        657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K


        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   P   P   C   P   A   P


        765         774         783         792         801         810
GAA GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   G   G   L   K   I   A   A   F   N   I   Q   T   F   G   E   T   K


        819         828         837         846         855         864
ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG AGC CGC TAC GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 M   S   N   A   T   L   V   S   Y   I   V   Q   I   L   S   R   Y   D


        873         882         891         900         909         918
ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC GTG GGG AAG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   A   L   V   Q   E   V   R   D   S   H   L   T   A   V   G   K   L


        927         936         945         954         963         972
CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y   V   V   S   E


        981         990         999        1008        1017        1026
CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   L   G   R   N   S   Y   K   E   R   Y   L   F   V   Y   R   P   D


       1035        1044        1053        1062        1071        1080
CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC GAG CCC TGC GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C   E   P   C   G


       1089        1098        1107        1116        1125        1134
AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC TCC CGG TTC ACA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 N   D   T   F   N   R   E   P   A   I   V   R   F   F   S   R   F   T


       1143        1152        1161        1170        1179        1188
GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG GGG GAC GCA GTA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   V   R   E   F   A   I   V   P   L   H   A   A   P   G   D   A   V


     1197        1206        1215        1224        1233        1242
```

```
GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA GAG AAA TGG GGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q   E   K   W   G

        1251        1260        1269        1278        1287        1296
TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC AGC TAT GTG AGA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   E   D   V   M   L   M   G   D   F   N   A   G   C   S   Y   V   R

        1305        1314        1323        1332        1341        1350
CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC TTC CAG TGG CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   S   Q   W   S   S   I   R   L   W   T   S   P   T   F   Q   W   L

        1359        1368        1377        1386        1395        1404
ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT GCC TAT GAC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   P   D   S   A   D   T   T   A   T   P   T   H   C   A   Y   D   R

        1413        1422        1431        1440        1449        1458
ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC GAC TCG GCT CTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   V   V   A   G   M   L   L   R   G   A   V   V   P   D   S   A   L

        1467        1476        1485        1494        1503        1512
CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG GCC CAA GCC ATC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L   A   Q   A   I

        1521        1530        1539        1548        1557        1566
AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA CCC AAA AAG AAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   D   H   Y   P   V   E   V   M   L   K   G   G   G   P   K   K   K

        1575
CGC AAG GTT TGA 3'
--- --- --- ---
 R   K   V   *
```

Figure 18

(A) pAS106

```
LOCUS        PAS106.DNA    1596 bp     mRNA            PRI        06-MAR-1995
DEFINITION   Humanised HMFG1 Fab'2 fused to human DNase I with SV40 NLS(pAS106)
ACCESSION
NID
KEYWORDS     DNase I.
SOURCE       DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM   Homo sapiens
             Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
             Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS    Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE      Recombinant human DNase I reduces the viscosity of cystic fibrosis
             sputum
  JOURNAL    Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE    91067672
BASE COUNT      355 a    475 c    452 g    314 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCTG TGTGGAGTGC CCACCGTGCC CAGCACCTGA AGGGAGCGGC
 781 GGGCTGAAGA TCGCAGCCTT CAACATCCAG ACATTTGGGG AGACCAAGAT GTCCAATGCC
 841 ACCCTCGTCA GCTACATTGT GCAGATCCTG AGCCGCTACG ACATCGCCCT GGTCCAGGAG
 901 GTCAGAGACA GCCACCTGAC TGCCGTGGGG AAGCTGCTGG ACAACCTCAA TCAGGACGCA
 961 CCAGACACCT ATCACTACGT GGTCAGTGAG CCACTGGGAC GGAACAGCTA TAAGGAGCGC
1021 TACCTGTTCG TGTACAGGCC TGACCAGGTG TCTGCGGTGG ACAGCTACTA CTACGATGAT
1081 GGCTGCGAGC CCTGCGGGAA CGACACCTTC AACCGAGAGC CAGCCATTGT CAGGTTCTTC
1141 TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC ATTGTTCCCC TGCATGCGGC CCCGGGGGAC
1201 GCAGTAGCCG AGATCGACGC TCTCTATGAC GTCTACCTGG ATGTCCAAGA GAAATGGGGC
1261 TTGGAGGACG TCATGTTGAT GGGCGACTTC AATGCGGGCT GCAGCTATGT GAGACCCTCC
1321 CAGTGGTCAT CCATCCGCCT GTGGACAAGC CCCACCTTCC AGTGGCTGAT CCCCGACAGC
1381 GCTGACACCA CAGCTACACC CACGCACTGT GCCTATGACA GGATCGTGGT TGCAGGGATG
1441 CTGCTCCGAG GGCCCGTTGT TCCCGACTCG GCTCTTCCCT TTAACTTCCA GGCTGCCTAT
1501 GGCCTGAGTG ACCAACTGGC CCAAGCCATC AGTGACCACT ATCCAGTGGA GGTGATGCTG
1561 AAGGGGGGCG GACCCAAAAA GAAGCGCAAG GTTTGA
```

↳ NLS

//

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Figure 18(B)

```
 CUS        FDDNASE106   1596 BP SS-DNA           SYN        25-AUG-2000
 FINITION   -
 CESSION    -
 EYWORDS    -
 OURCE      -
 ATURES                  Location/Qualifiers
      frag               join(1..>720,<799..1596)
                         /note="1 to 1596 of PAS106.dna [Split]"
      frag               721..798
                         /note="1 to 78 of 102/106linker"
BASE COUNT      355 A    474 C    452 G    315 T        0 OTHER
ORIGIN      -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTCGAGTGT CCACCGTGTC CAGCACCAGA GGGGAGCGGC
      781 GGGCTGAAGA TCGCAGCCTT CAACATCCAG ACATTTGGGG AGACCAAGAT GTCCAATGCC
      841 ACCCTCGTCA GCTACATTGT GCAGATCCTG AGCCGCTACG ACATCGCCCT GGTCCAGGAG
      901 GTCAGAGACA GCCACCTGAC TGCCGTGGGG AAGCTGCTGG ACAACCTCAA TCAGGACGCA
      961 CCAGACACCT ATCACTACGT GGTCAGTGAG CCACTGGGAC GGAACAGCTA TAAGGAGCGC
     1021 TACCTGTTCG TGTACAGGCC TGACCAGGTG TCTGCGGTGG ACAGCTACTA CTACGATGAT
     1081 GGCTGCGAGC CCTGCGGGAA CGACACCTTC AACCGAGAGC CAGCCATTGT CAGGTTCTTC
     1141 TCCCGGTTCA CAGAGGTCAG GGAGTTTGCC ATTGTTCCCC TGCATGCGGC CCCGGGGGAC
     1201 GCAGTAGCCG AGATCGACGC TCTCTATGAC GTCTACCTGG ATGTCCAAGA GAAATGGGGC
     1261 TTGGAGGACG TCATGTTGAT GGGCGACTTC AATGCGGGCT GCAGCTATGT GAGACCCTCC
     1321 CAGTGGTCAT CCATCCGCCT GTGGACAAGC CCCACCTTCC AGTGGCTGAT CCCCGACAGC
     1381 GCTGACACCA CAGCTACACC CACGCACTGT GCCTATGACA GGATCGTGGT TGCAGGGATG
     1441 CTGCTCCGAG GGGCCGTTGT TCCCGACTCG GCTCTTCCCT TTAACTTCCA GGCTGCCTAT
     1501 GGCCTGAGTG ACCAACTGGC CCAAGCCATC AGTGACCACT ATCCAGTGGA GGTGATGCTG
     1561 AAGGGGGGCG GACCCAAAAA GAAGCGCAAG GTTTGA
```

Figure 18(c)

```
LOCUS         FDDNASE106   1605 BP SS-DNA          SYN       29-AUG-2000
DEFINITION    -
ACCESSION     -
KEYWORDS      -
SOURCE        -
FEATURES                   Location/Qualifiers
       frag                10..1605
                           /note="1 to 1596 of FdDNase106correct"
       frag                join(10..>729,<808..1605)
                           /note="1 to 1596 of PAS106.dna [Split]"
       frag                730..807
                           /note="1 to 78 of 102/106linker"
BASE COUNT       356 A     480 C     454 G     315 T      0 OTHER
ORIGIN        -
         1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
        61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
       121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
       181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
       241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
       301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
       361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
       421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
       481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
       541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
       601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
       661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
       721 AAATCTTGTG ACAAAACTCA CACATGCTGT GTCGAGTGTC CACCGTGTCC AGCACCAGAG
       781 GGGAGCGGCG GGCTGAAGAT CGCAGCCTTC AACATCCAGA CATTTGGGGA GACCAAGATG
       841 TCCAATGCCA CCCTCGTCAG CTACATTGTG CAGATCCTGA GCCGCTACGA CATCGCCCTG
       901 GTCCAGGAGG TCAGAGACAG CCACCTGACT GCCGTGGGGA AGCTGCTGGA CAACCTCAAT
       961 CAGGACGCAC CAGACACCTA TCACTACGTG GTCAGTGAGC CACTGGGACG GAACAGCTAT
      1021 AAGGAGCGCT ACCTGTTCGT GTACAGGCCT GACCAGGTGT CTGCGGTGGA CAGCTACTAC
      1081 TACGATGATG GCTGCGAGCC CTGCGGGAAC GACACCTTCA ACCGAGAGCC AGCCATTGTC
      1141 AGGTTCTTCT CCCGGTTCAC AGAGGTCAGG GAGTTTGCCA TTGTTCCCCT GCATGCGGCC
      1201 CCGGGGGACG CAGTAGCCGA GATCGACGCT CTCTATGACG TCTACCTGGA TGTCCAAGAG
      1261 AAATGGGGCT TGGAGGACGT CATGTTGATG GGCGACTTCA ATGCGGGCTG CAGCTATGTG
      1321 AGACCCTCCC AGTGGTCATC CATCCGCCTG TGGACAAGCC CCACCTTCCA GTGGCTGATC
      1381 CCCGACAGCG CTGACACCAC AGCTACACCC ACGCACTGTG CCTATGACAG GATCGTGGTT
      1441 GCAGGGATGC TGCTCCGAGG GGCCGTTGTT CCCGACTCGG CTCTTCCCTT TAACTTCCAG
      1501 GCTGCCTATG GCCTGAGTGA CCAACTGGCC CAAGCCATCA GTGACCACTA TCCAGTGGAG
      1561 GTGATGCTGA AGGGGGGCGG ACCCAAAAAG AAGCGCAAGG TTTGA
//
```

```
              9              18             27             36             45             54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


              63             72             81             90             99            108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


             117            126            135            144            153            162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


             171            180            189            198            207            216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


             225            234            243            252            261            270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


             279            288            297            306            315            324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


             333            342            351            360            369            378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


             387            396            405            414            423            432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


             441            450            459            468            477            486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


             495            504            513            522            531            540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


             549            558            567            576            585            594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

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```
      603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

      657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

      711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC TGT GTG GAG TGC CCA CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   C   V   E   C   P   P

      765         774         783         792         801         810
TGC CCA GCA CCT GAA GGG AGC GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   P   A   P   E   G   S   G   G   L   K   I   A   A   F   N   I   Q

      819         828         837         846         855         864
ACA TTT GGG GAG ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   F   G   E   T   K   M   S   N   A   T   L   V   S   Y   I   V   Q

      873         882         891         900         909         918
ATC CTG AGC CGC TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 I   L   S   R   Y   D   I   A   L   V   Q   E   V   R   D   S   H   L

      927         936         945         954         963         972
ACT GCC GTG GGG AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   A   V   G   K   L   L   D   N   L   N   Q   D   A   P   D   T   Y

      981         990         999        1008        1017        1026
CAC TAC GTG GTC AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 H   Y   V   V   S   E   P   L   G   R   N   S   Y   K   E   R   Y   L

     1035        1044        1053        1062        1071        1080
TTC GTG TAC AGG CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   V   Y   R   P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D

     1089        1098        1107        1116        1125        1134
GGC TGC GAG CCC TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   C   E   P   C   G   N   D   T   F   N   R   E   P   A   I   V   R

     1143        1152        1161        1170        1179        1188
TTC TTC TCC CGG TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   F   S   R   F   T   E   V   R   E   F   A   I   V   P   L   H   A

     1197        1206        1215        1224        1233        1242
```

-2-

```
GCC CCG GGG GAC GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   P   G   D   A   V   A   E   I   D   A   L   Y   D   V   Y   L   D

        1251        1260        1269        1278        1287        1296
GTC CAA GAG AAA TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   Q   E   K   W   G   L   E   D   V   M   L   M   G   D   F   N   A

        1305        1314        1323        1332        1341        1350
GGC TGC AGC TAT GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   C   S   Y   V   R   P   S   Q   W   S   S   I   R   L   W   T   S

        1359        1368        1377        1386        1395        1404
CCC ACC TTC CAG TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 P   T   F   Q   W   L   I   P   D   S   A   D   T   T   A   T   P   T

        1413        1422        1431        1440        1449        1458
CAC TGT GCC TAT GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 H   C   A   Y   D   R   I   V   V   A   G   M   L   L   R   G   A   V

        1467        1476        1485        1494        1503        1512
GTT CCC GAC TCG GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   P   D   S   A   L   P   F   N   F   Q   A   A   Y   G   L   S   D

        1521        1530        1539        1548        1557        1566
CAA CTG GCC CAA GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Q   L   A   Q   A   I   S   D   H   Y   P   V   E   V   M   L   K   G

        1575        1584        1593
GGC GGA CCC AAA AAG AAG CGC AAG GTT TGA 3'
--- --- --- --- --- --- --- --- --- ---
 G   G   P   K   K   K   R   K   V   *
```

FIGURE 19

(h) pAS107

```
LOCUS       PAS107.DNA    1590 bp      mRNA             PRI         06-MAR-1995
DEFINITION  Humanised HMFG1 Fab'2 fused to human DNase I with SV40 NLS(pAS107)
ACCESSION
NID
KEYWORDS    DNase I.
SOURCE      DNase I sequence is from assembled oligos (thus modified c/f
MHDNASE1.dna)
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
  AUTHORS   Shak,S., Capon,D.J., Hellmiss,R., Marsters,S.A. and Baker,C.L.
  TITLE     Recombinant human DNase I reduces the viscosity of cystic fibrosis
            sputum
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 87 (23), 9188-9192 (1990)
  MEDLINE   91067672
BASE COUNT      354 a    474 c    448 g    314 t
ORIGIN
```

```
   1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
  61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGCCTCAGT GAAGGTGTCC
 121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
 181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
 241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
 301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
 361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
 421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
 481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
 541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
 601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
 661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
 721 GACAAAACTC ACACATGCTG TGTGGAGTGC CCACCGTGCC CAGCACCTGA AGGCGGGCTG
 781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
 841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
 901 GACAGCCACC TGACTGCCGT GGGGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
 961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA CGCGCTACCTG
1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
1081 GAGCCCTGCG GGAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGGGG
1561 GGCGGACCCA AAAAGAAGCG CAAGGTTTGA
//
```

└→ NLS

Figure 19 (B)

```
LOCUS       FDDNASE107   1590 BP SS-DNA             SYN        25-AUG-2000
DEFINITION  -
ACCESSION   -
KEYWORDS    -
SOURCE      -
FEATURES              Location/Qualifiers
     frag             join(1..>720,<793..1590)
                      /note="1 to 1590 of PAS107.dna [Split]"
     frag             721..792
                      /note="1 to 72 of 103/107linker"
     frag             join(721..>771,<772..792)
                      /note="1 to 78 of 102linker [Split]"
BASE COUNT     354 A    473 C    448 G    315 T       0 OTHER
ORIGIN       -
        1 ATGGGATGGA GCTGTATCAT CCTCTTCTTG GTAGCAACAG CTACAGGTGT CCACTCCCAG
       61 GTGCAGCTGG TGCAGTCTGG GGCAGAGGTG AAAAAGCCTG GGGCCTCAGT GAAGGTGTCC
      121 TGCAAGGCTT CTGGCTACAC CTTCAGTGCC TACTGGATAG AGTGGGTGCG CCAGGCTCCA
      181 GGAAAGGGCC TCGAGTGGGT CGGAGAGATT TTACCTGGAA GTAATAATTC TAGATACAAT
      241 GAGAAGTTCA AGGGCCGAGT GACAGTCACT AGAGACACAT CCACAAACAC AGCCTACATG
      301 GAGCTCAGCA GCCTGAGGTC TGAGGACACA GCCGTCTATT ACTGTGCAAG ATCCTACGAC
      361 TTTGCCTGGT TTGCTTACTG GGGCCAAGGG ACTCTGGTCA CAGTCTCCTC AGCCTCCACC
      421 AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG
      481 GCCCTGGGCT GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTGTC GTGGAACTCA
      541 GGCGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCCTC AGGACTCTAC
      601 TCCCTCAGCA GCGTGGTGAC CGTGCCCTCC AGCAGCTTGG GCACCCAGAC CTACATCTGC
      661 AACGTGAATC ACAAGCCCAG CAACACCAAG GTGGACAAGA AAGTTGAGCC CAAATCTTGT
      721 GACAAAACTC ACACATGCTG TGTCGAGTGT CCACCGTGTC CAGCACCAGA GGGCGGGCTG
      781 AAGATCGCAG CCTTCAACAT CCAGACATTT GGGGAGACCA AGATGTCCAA TGCCACCCTC
      841 GTCAGCTACA TTGTGCAGAT CCTGAGCCGC TACGACATCG CCCTGGTCCA GGAGGTCAGA
      901 GACAGCCACC TGACTGCCGT GGGGAAGCTG CTGGACAACC TCAATCAGGA CGCACCAGAC
      961 ACCTATCACT ACGTGGTCAG TGAGCCACTG GGACGGAACA GCTATAAGGA GCGCTACCTG
     1021 TTCGTGTACA GGCCTGACCA GGTGTCTGCG GTGGACAGCT ACTACTACGA TGATGGCTGC
     1081 GAGCCCTGCG GGAACGACAC CTTCAACCGA GAGCCAGCCA TTGTCAGGTT CTTCTCCCGG
     1141 TTCACAGAGG TCAGGGAGTT TGCCATTGTT CCCCTGCATG CGGCCCCGGG GGACGCAGTA
     1201 GCCGAGATCG ACGCTCTCTA TGACGTCTAC CTGGATGTCC AAGAGAAATG GGGCTTGGAG
     1261 GACGTCATGT TGATGGGCGA CTTCAATGCG GGCTGCAGCT ATGTGAGACC CTCCCAGTGG
     1321 TCATCCATCC GCCTGTGGAC AAGCCCCACC TTCCAGTGGC TGATCCCCGA CAGCGCTGAC
     1381 ACCACAGCTA CACCCACGCA CTGTGCCTAT GACAGGATCG TGGTTGCAGG GATGCTGCTC
     1441 CGAGGGGCCG TTGTTCCCGA CTCGGCTCTT CCCTTTAACT TCCAGGCTGC CTATGGCCTG
     1501 AGTGACCAAC TGGCCCAAGC CATCAGTGAC CACTATCCAG TGGAGGTGAT GCTGAAGGGG
     1561 GGCGGACCCA AAAAGAAGCG CAAGGTTTGA
```

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Figure 19 (C)

```
LOCUS        FDDNASE107    1599 BP SS-DNA              SYN        29-AUG-2000
DEFINITION   -
ACCESSION    -
KEYWORDS     -
SOURCE       -
FEATURES                   Location/Qualifiers
     frag                  10..1599
                           /note="1 to 1590 of FdDNase107correct"
     frag                  join(10..>729,<802..1599)
                           /note="1 to 1590 of PAS107.dna [Split]"
     frag                  730..801
                           /note="1 to 72 of 103/107linker"
     frag                  join(730..>780,<781..801)
                           /note="1 to 78 of 102linker [Split]"
BASE COUNT        355 A      479 C      450 G      315 T      0 OTHER
ORIGIN       -
        1 GCCGCCACCA TGGGATGGAG CTGTATCATC CTCTTCTTGG TAGCAACAGC TACAGGTGTC
       61 CACTCCCAGG TGCAGCTGGT GCAGTCTGGG GCAGAGGTGA AAAAGCCTGG GGCCTCAGTG
      121 AAGGTGTCCT GCAAGGCTTC TGGCTACACC TTCAGTGCCT ACTGGATAGA GTGGGTGCGC
      181 CAGGCTCCAG GAAAGGGCCT CGAGTGGGTC GGAGAGATTT TACCTGGAAG TAATAATTCT
      241 AGATACAATG AGAAGTTCAA GGGCCGAGTG ACAGTCACTA GAGACACATC CACAAACACA
      301 GCCTACATGG AGCTCAGCAG CCTGAGGTCT GAGGACACAG CCGTCTATTA CTGTGCAAGA
      361 TCCTACGACT TTGCCTGGTT TGCTTACTGG GGCCAAGGGA CTCTGGTCAC AGTCTCCTCA
      421 GCCTCCACCA AGGGCCCATC GGTCTTCCCC CTGGCACCCT CCTCCAAGAG CACCTCTGGG
      481 GGCACAGCGG CCCTGGGCTG CCTGGTCAAG GACTACTTCC CCGAACCGGT GACGGTGTCG
      541 TGGAACTCAG GCGCCCTGAC CAGCGGCGTG CACACCTTCC CGGCTGTCCT ACAGTCCTCA
      601 GGACTCTACT CCCTCAGCAG CGTGGTGACC GTGCCCTCCA GCAGCTTGGG CACCCAGACC
      661 TACATCTGCA ACGTGAATCA CAAGCCCAGC AACACCAAGG TGGACAAGAA AGTTGAGCCC
      721 AAATCTTGTG ACAAAACTCA CACATGCTGT GTCGAGTGTC CACCGTGTCC AGCACCAGAG
      781 GGCGGGCTGA AGATCGCAGC CTTCAACATC CAGACATTTG GGAGACCAA GATGTCCAAT
      841 GCCACCCTCG TCAGCTACAT TGTGCAGATC CTGAGCCGCT ACGACATCGC CCTGGTCCAG
      901 GAGGTCAGAG ACAGCCACCT GACTGCCGTG GGGAAGCTGC TGGACAACCT CAATCAGGAC
      961 GCACCAGACA CCTATCACTA CGTGGTCAGT GAGCCACTGG GACGGAACAG CTATAAGGAG
     1021 CGCTACCTGT TCGTGTACAG GCCTGACCAG GTGTCTGCGG TGGACAGCTA CTACTACGAT
     1081 GATGGCTGCG AGCCCTGCGG GAACGACACC TTCAACCGAG AGCCAGCCAT TGTCAGGTTC
     1141 TTCTCCCGGT TCACAGAGGT CAGGGAGTTT GCCATTGTTC CCCTGCATGC GGCCCCGGGG
     1201 GACGCAGTAG CCGAGATCGA CGCTCTCTAT GACGTCTACC TGGATGTCCA AGAGAAATGG
     1261 GGCTTGGAGG ACGTCATGTT GATGGGCGAC TTCAATGCGG CTGCAGCTA TGTGAGACCC
     1321 TCCCAGTGGT CATCCATCCG CCTGTGGACA AGCCCCACCT TCCAGTGGCT GATCCCCGAC
     1381 AGCGCTGACA CCACAGCTAC ACCCACGCAC TGTGCCTATG ACAGGATCGT GGTTGCAGGG
     1441 ATGCTGCTCC GAGGGGCCGT TGTTCCCGAC TCGGCTCTTC CCTTTAACTT CCAGGCTGCC
     1501 TATGGCCTGA GTGACCAACT GGCCCAAGCC ATCAGTGACC ACTATCCAGT GGAGGTGATG
     1561 CTGAAGGGGG GCGGACCCAA AAAGAAGCGC AAGGTTTGA
//
```

FIGURE 19 (1)

```
            9           18           27           36           45           54
5'  ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA GCT ACA GGT GTC CAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     M   G   W   S   C   I   I   L   F   L   V   A   T   A   T   G   V   H


            63          72           81           90           99          108
    TCC CAG GTG CAG CTG GTG CAG TCT GGG GCA GAG GTG AAA AAG CCT GGG GCC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G   A   S


            117         126          135          144          153         162
    GTG AAG GTG TCC TGC AAG GCT TCT GGC TAC ACC TTC AGT GCC TAC TGG ATA GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   K   V   S   C   K   A   S   G   Y   T   F   S   A   Y   W   I   E


            171         180          189          198          207         216
    TGG GTG CGC CAG GCT CCA GGA AAG GGC CTC GAG TGG GTC GGA GAG ATT TTA CCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   V   R   Q   A   P   G   K   G   L   E   W   V   G   E   I   L   P


            225         234          243          252          261         270
    GGA AGT AAT AAT TCT AGA TAC AAT GAG AAG TTC AAG GGC CGA GTG ACA GTC ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   S   N   N   S   R   Y   N   E   K   F   K   G   R   V   T   V   T


            279         288          297          306          315         324
    AGA GAC ACA TCC ACA AAC ACA GCC TAC ATG GAG CTC AGC AGC CTG AGG TCT GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     R   D   T   S   T   N   T   A   Y   M   E   L   S   S   L   R   S   E


            333         342          351          360          369         378
    GAC ACA GCC GTC TAT TAC TGT GCA AGA TCC TAC GAC TTT GCC TGG TTT GCT TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     D   T   A   V   Y   Y   C   A   R   S   Y   D   F   A   W   F   A   Y


            387         396          405          414          423         432
    TGG GGC CAA GGG ACT CTG GTC ACA GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S


            441         450          459          468          477         486
    GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA GCG GCC CTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     V   F   P   L   A   P   S   S   K   S   T   S   G   G   T   A   A   L


            495         504          513          522          531         540
    GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   C   L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S


            549         558          567          576          585         594
    GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
     G   A   L   T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G
```

- 1 -

```
        603         612         621         630         639         648
CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 L   Y   S   L   S   S   V   V   T   V   P   S   S   S   L   G   T   Q

        657         666         675         684         693         702
ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 T   Y   I   C   N   V   N   H   K   P   S   N   T   K   V   D   K   K

        711         720         729         738         747         756
GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGC TGT GTG GAG TGC CCA CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   E   P   K   S   C   D   K   T   H   T   C   C   V   E   C   P   P

        765         774         783         792         801         810
TGC CCA GCA CCT GAA GGC GGG CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 C   P   A   P   E   G   G   L   K   I   A   A   F   N   I   Q   T   F

        819         828         837         846         855         864
GGG GAG ACC AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   E   T   K   M   S   N   A   T   L   V   S   Y   I   V   Q   I   L

        873         882         891         900         909         918
AGC CGC TAC GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC CTG ACT GCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   R   Y   D   I   A   L   V   Q   E   V   R   D   S   H   L   T   A

        927         936         945         954         963         972
GTG GGG AAG CTG CTG GAC AAC CTC AAT CAG GAC GCA CCA GAC ACC TAT CAC TAC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   G   K   L   L   D   N   L   N   Q   D   A   P   D   T   Y   H   Y

        981         990         999        1008        1017        1026
GTG GTC AGT GAG CCA CTG GGA CGG AAC AGC TAT AAG GAG CGC TAC CTG TTC GTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 V   V   S   E   P   L   G   R   N   S   Y   K   E   R   Y   L   F   V

       1035        1044        1053        1062        1071        1080
TAC AGG CCT GAC CAG GTG TCT GCG GTG GAC AGC TAC TAC TAC GAT GAT GGC TGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 Y   R   P   D   Q   V   S   A   V   D   S   Y   Y   Y   D   D   G   C

       1089        1098        1107        1116        1125        1134
GAG CCC TGC GGG AAC GAC ACC TTC AAC CGA GAG CCA GCC ATT GTC AGG TTC TTC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   P   C   G   N   D   T   F   N   R   E   P   A   I   V   R   F   F

       1143        1152        1161        1170        1179        1188
TCC CGG TTC ACA GAG GTC AGG GAG TTT GCC ATT GTT CCC CTG CAT GCG GCC CCG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   R   F   T   E   V   R   E   F   A   I   V   P   L   H   A   A   P

       1197        1206        1215        1224        1233        1242
```

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```
GGG GAC GCA GTA GCC GAG ATC GAC GCT CTC TAT GAC GTC TAC CTG GAT GTC CAA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 G   D   A   V   A   E   I   D   A   L   Y   D   V   Y   L   D   V   Q

         1251        1260        1269        1278        1287        1296
GAG AAA TGG GGC TTG GAG GAC GTC ATG TTG ATG GGC GAC TTC AAT GCG GGC TGC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 E   K   W   G   L   E   D   V   M   L   M   G   D   F   N   A   G   C

         1305        1314        1323        1332        1341        1350
AGC TAT GTG AGA CCC TCC CAG TGG TCA TCC ATC CGC CTG TGG ACA AGC CCC ACC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 S   Y   V   R   P   S   Q   W   S   S   I   R   L   W   T   S   P   T

         1359        1368        1377        1386        1395        1404
TTC CAG TGG CTG ATC CCC GAC AGC GCT GAC ACC ACA GCT ACA CCC ACG CAC TGT
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 F   Q   W   L   I   P   D   S   A   D   T   T   A   T   P   T   H   C

         1413        1422        1431        1440        1449        1458
GCC TAT GAC AGG ATC GTG GTT GCA GGG ATG CTG CTC CGA GGG GCC GTT GTT CCC
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   Y   D   R   I   V   V   A   G   M   L   L   R   G   A   V   V   P

         1467        1476        1485        1494        1503        1512
GAC TCG GCT CTT CCC TTT AAC TTC CAG GCT GCC TAT GGC CTG AGT GAC CAA CTG
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 D   S   A   L   P   F   N   F   Q   A   A   Y   G   L   S   D   Q   L

         1521        1530        1539        1548        1557        1566
GCC CAA GCC ATC AGT GAC CAC TAT CCA GTG GAG GTG ATG CTG AAG GGG GGC GGA
--- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
 A   Q   A   I   S   D   H   Y   P   V   E   V   M   L   K   G   G   G

         1575        1584
CCC AAA AAG AAG CGC AAG GTT TGA 3'
--- --- --- --- --- --- --- ---
 P   K   K   K   R   K   V   *
```

FIG 20

Mammalian expression of humanised HMFG1-DNase constructs
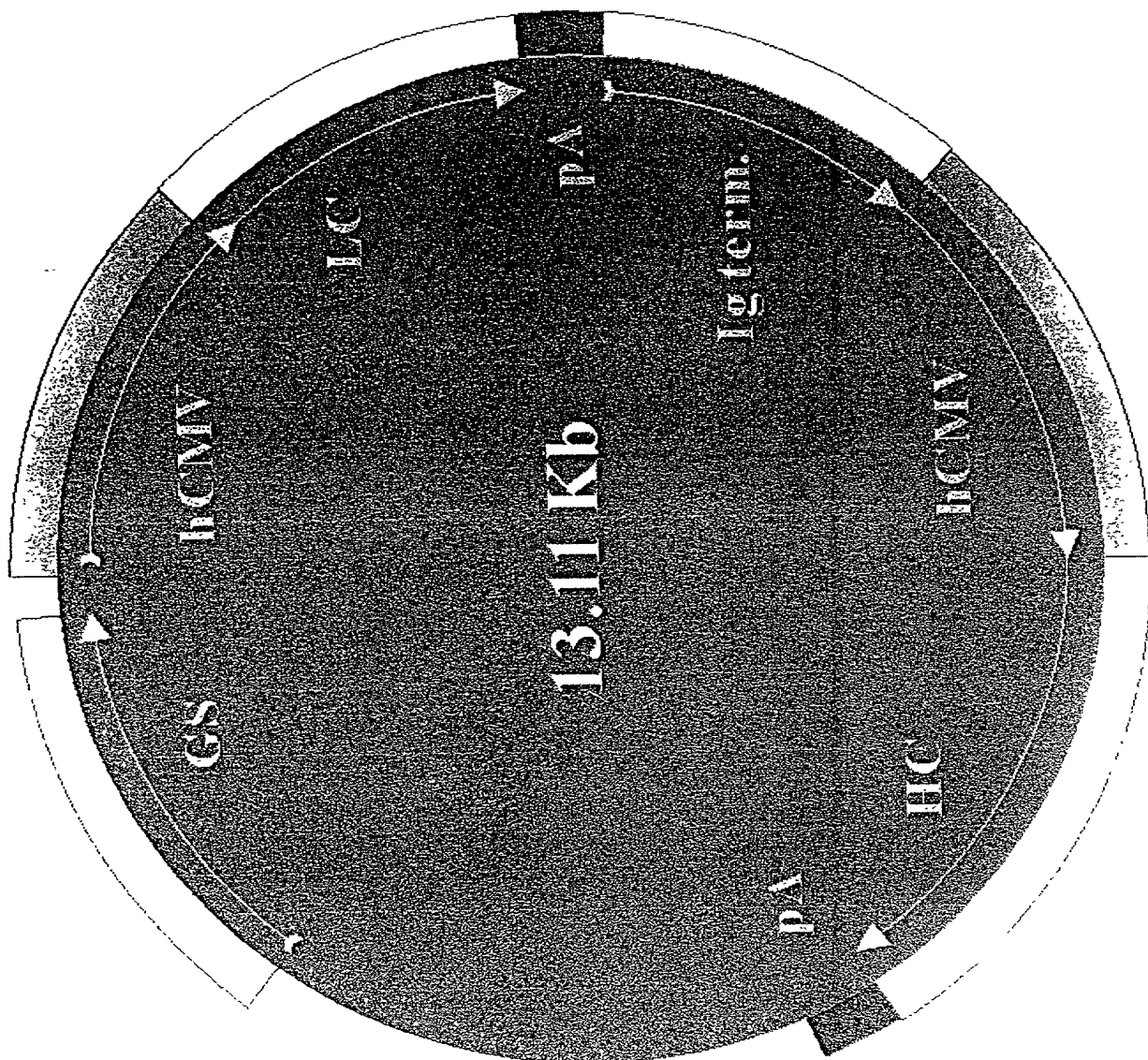
FIG 21(A) Immuno-precipitation of metabolically labelled transient transfectants
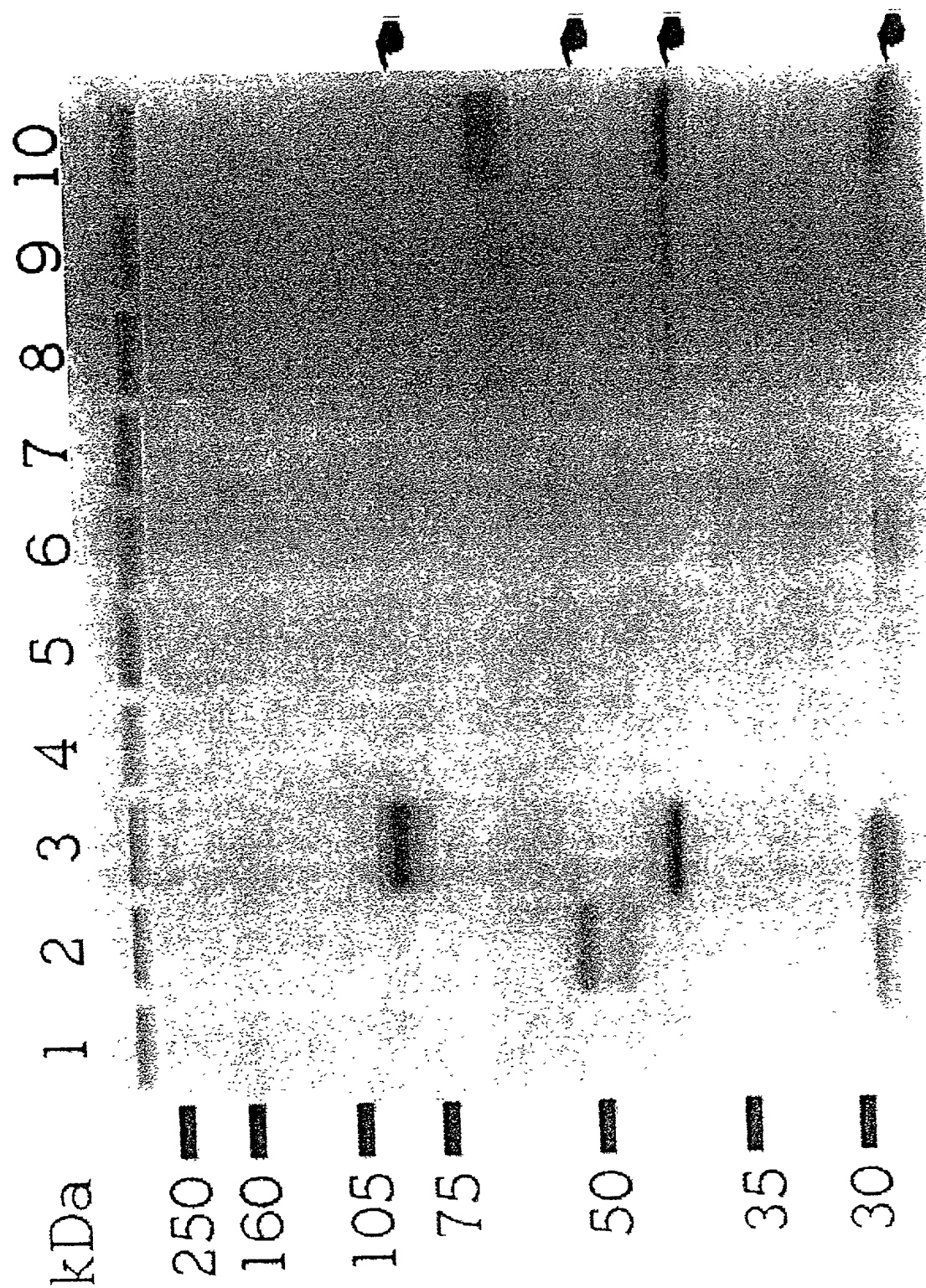
kDa 1 2 3 4 5 6 7 8 9 10

250
160
105
75
50
35
30

8% SDS-PAGE reducing gel

FIG 21

Fig 21 (B)

Immuno-precipitation of metabolically labelled transient transfectants

SDS PAGE non-reducing gel

FIG 21

(c) Immuno-precipitation of metabolically labelled transient transfectants

1 2 3 4 5 6 7 8 9 10 11

250
160
105
75

50

35

30
25

15

10% SDS-PAGE reducing gel

FIG 2I   Immuno-precipitation of metabolically labelled transient transfectants

(i) kDa

1 2 3 4 5 6 7 8 9 10 11

250
160
105
75
50
35
30
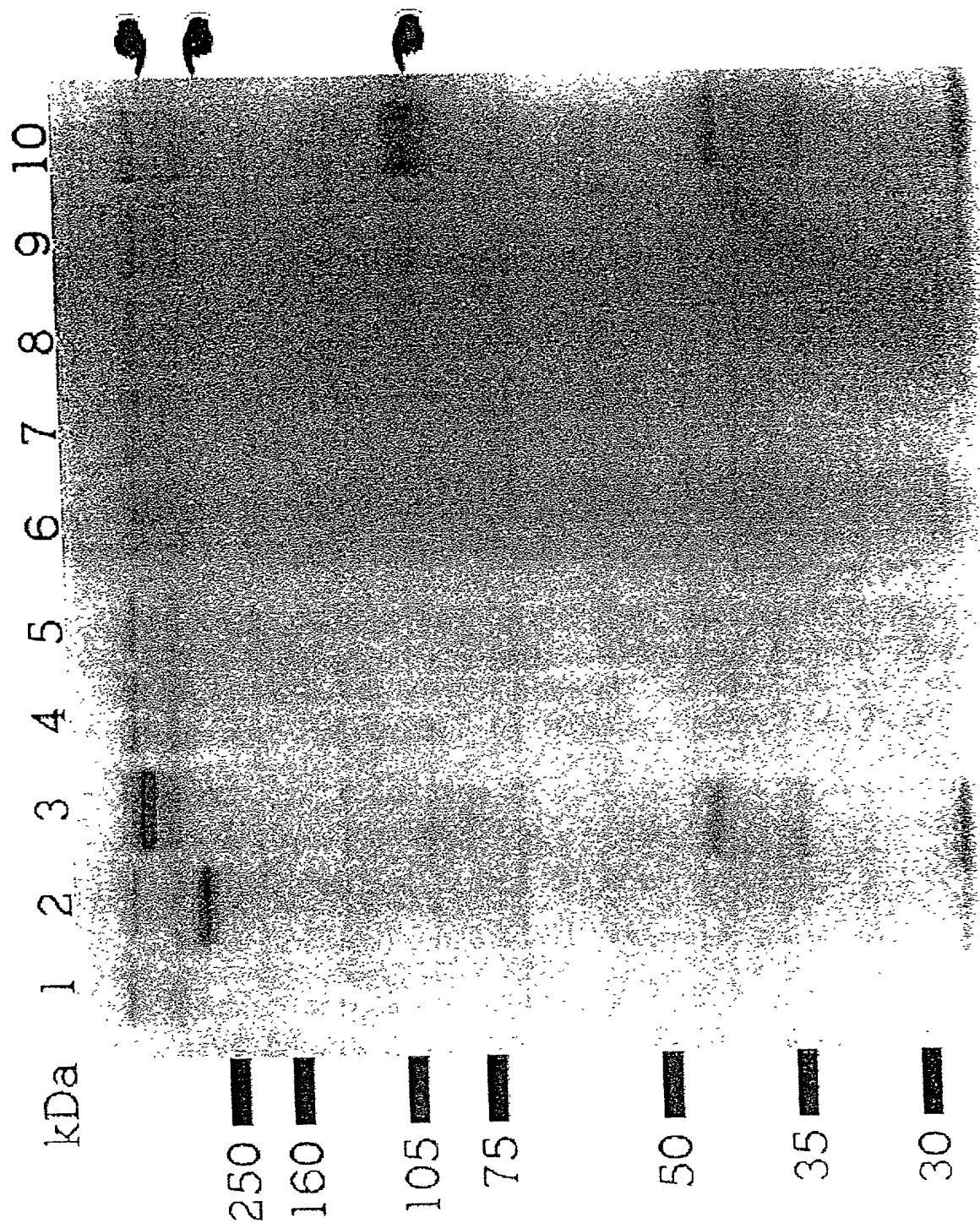
8% SDS-PAGE non-reducing gel
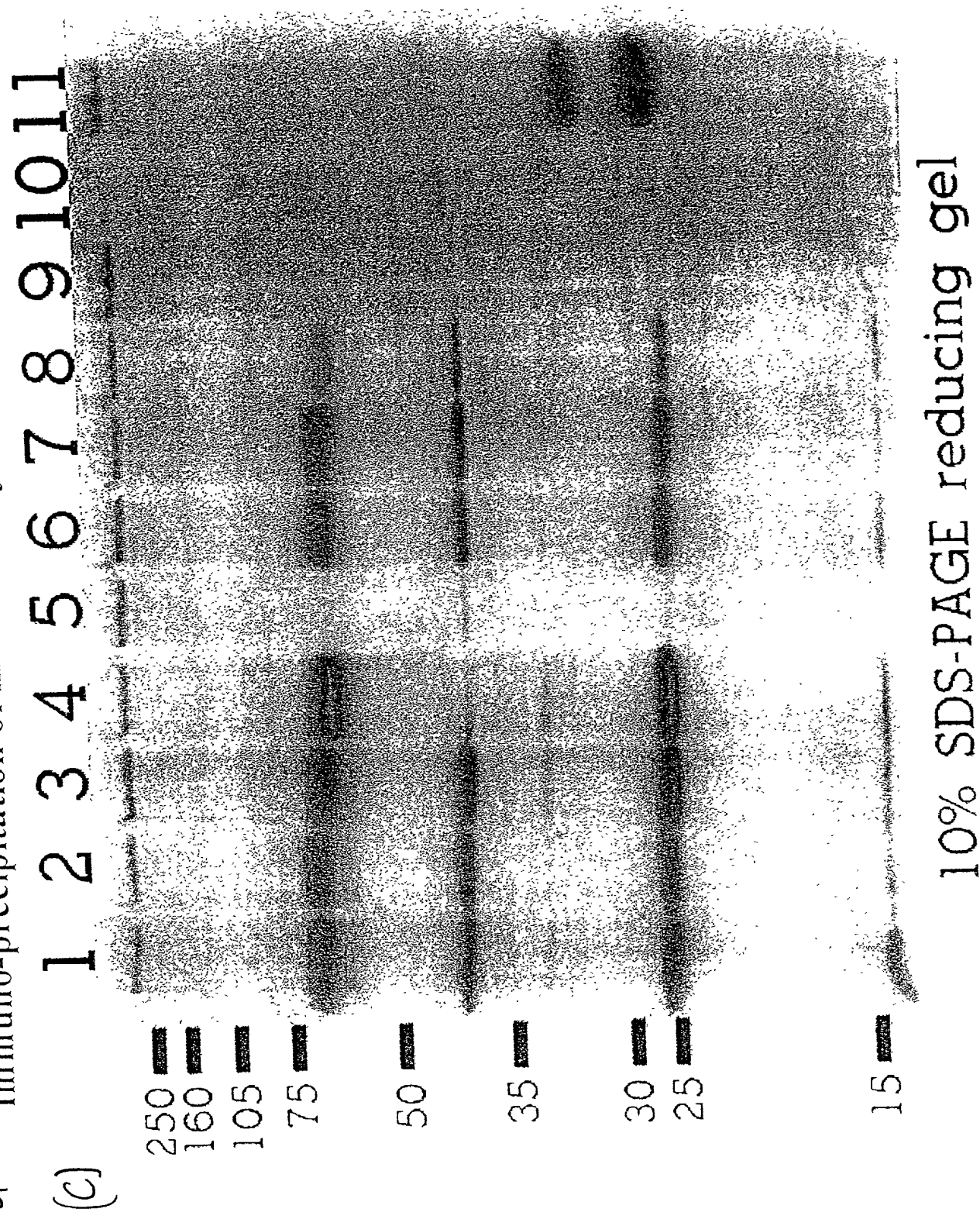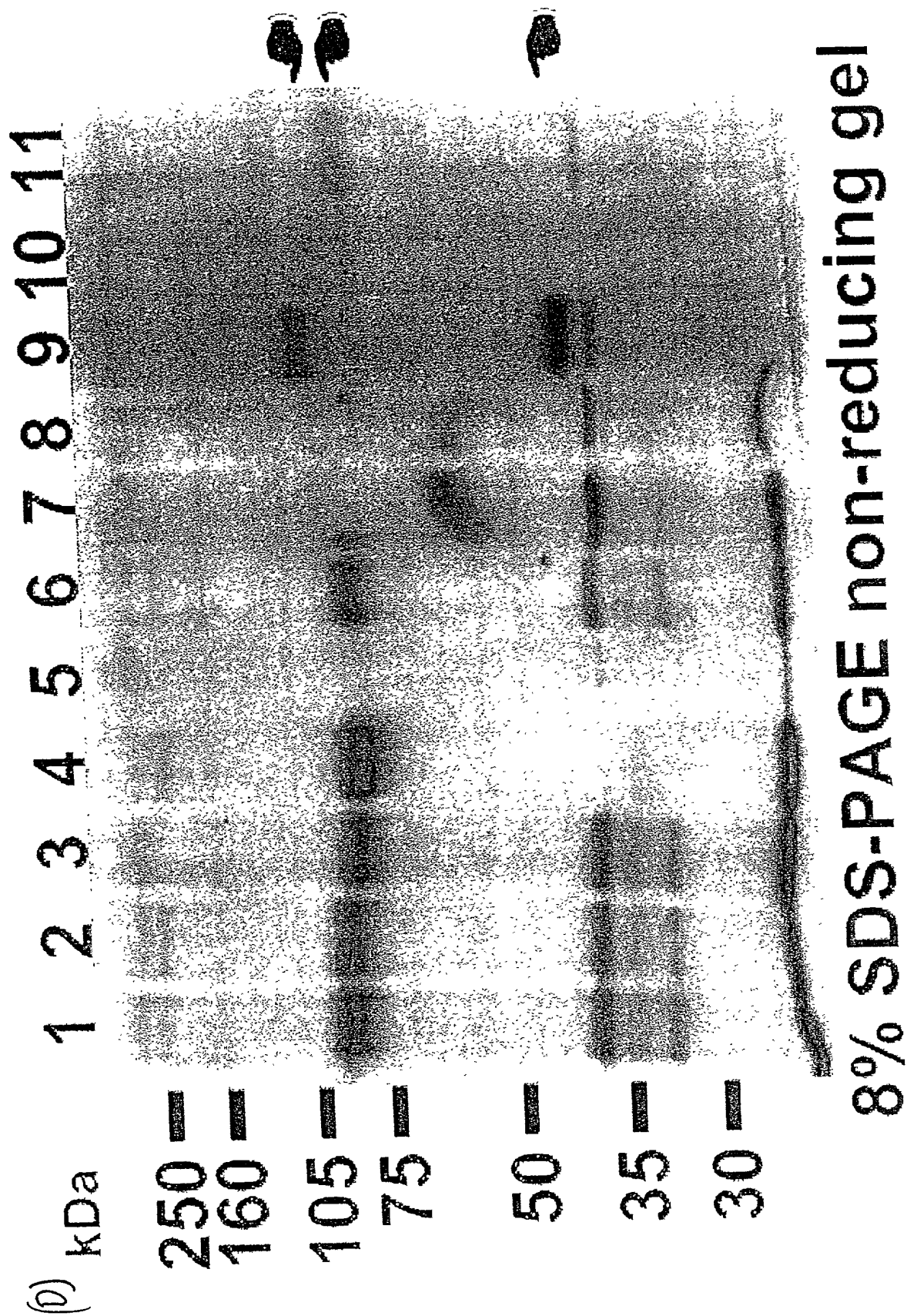
PDTRP binding assay standard curve
(5' development)

Sigmoidal(Boltzman) fit to hHMFG1 5min_mean OD
Boltzman
x0 center dx width
A1 Y initial A2 Y final
(A1-A2)/ (1+exp((x-x0)/dx)) + A2

chisq/= 23.80157

init(A1) = 2.6131 ± 0.0308
final(A2) = -4.9089 ± 1.35
X at Y50(x0) = -0.8970 ± 0.335
Width(dx) = -1.0871 ± 0.0770

X at Y20 = 0.80997
X at Y80 = -2.204

OD 630 nm

Concentration of humanised HMFG1 (µg/ml)

FIG 22
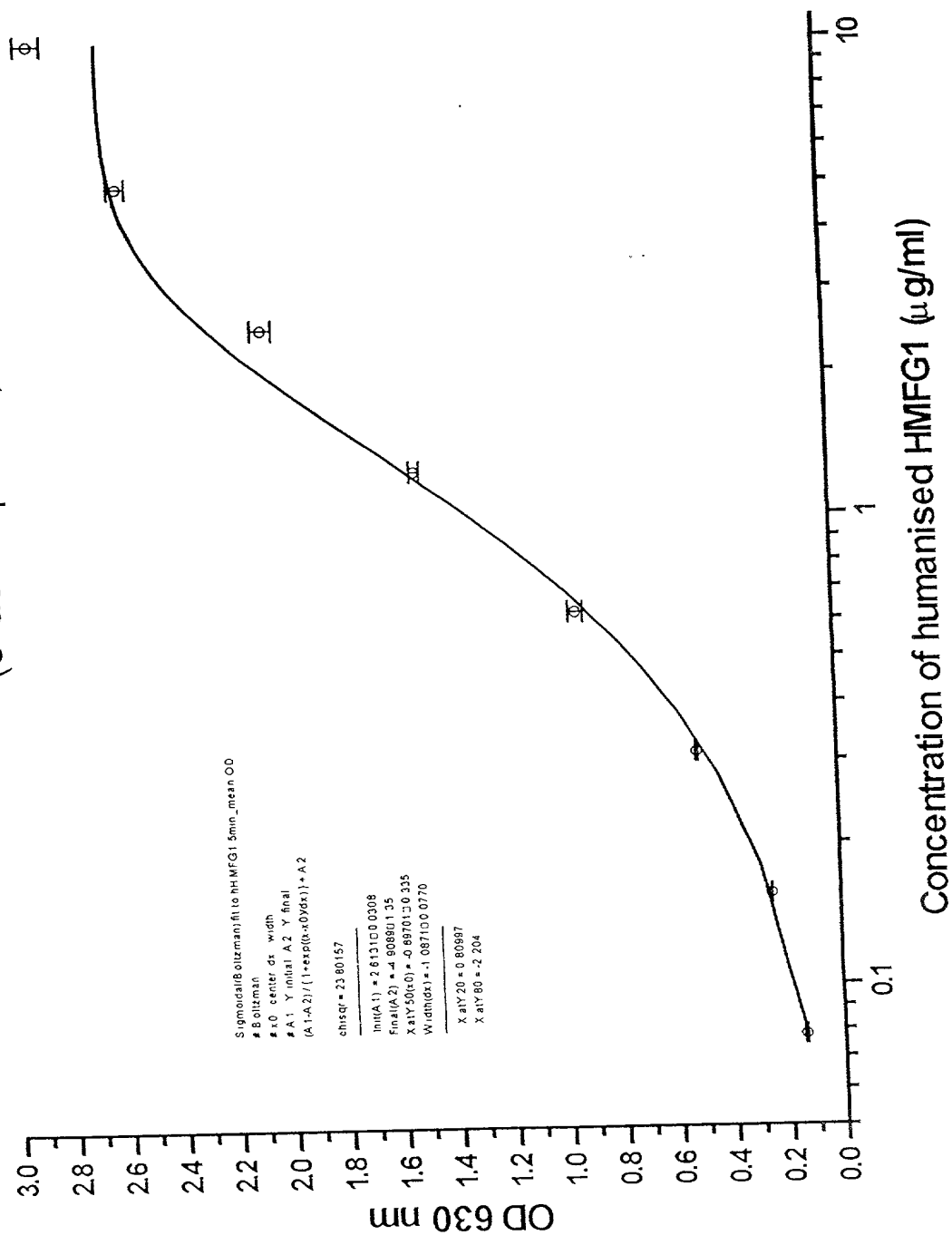
Corrected bovine DNase I standard curves at various time points

Bovine DNase I concentration (nM)

Corrected OD 620 nm

1 hour
2 hour
3 hour
4 hour
5 hour

FIG 23
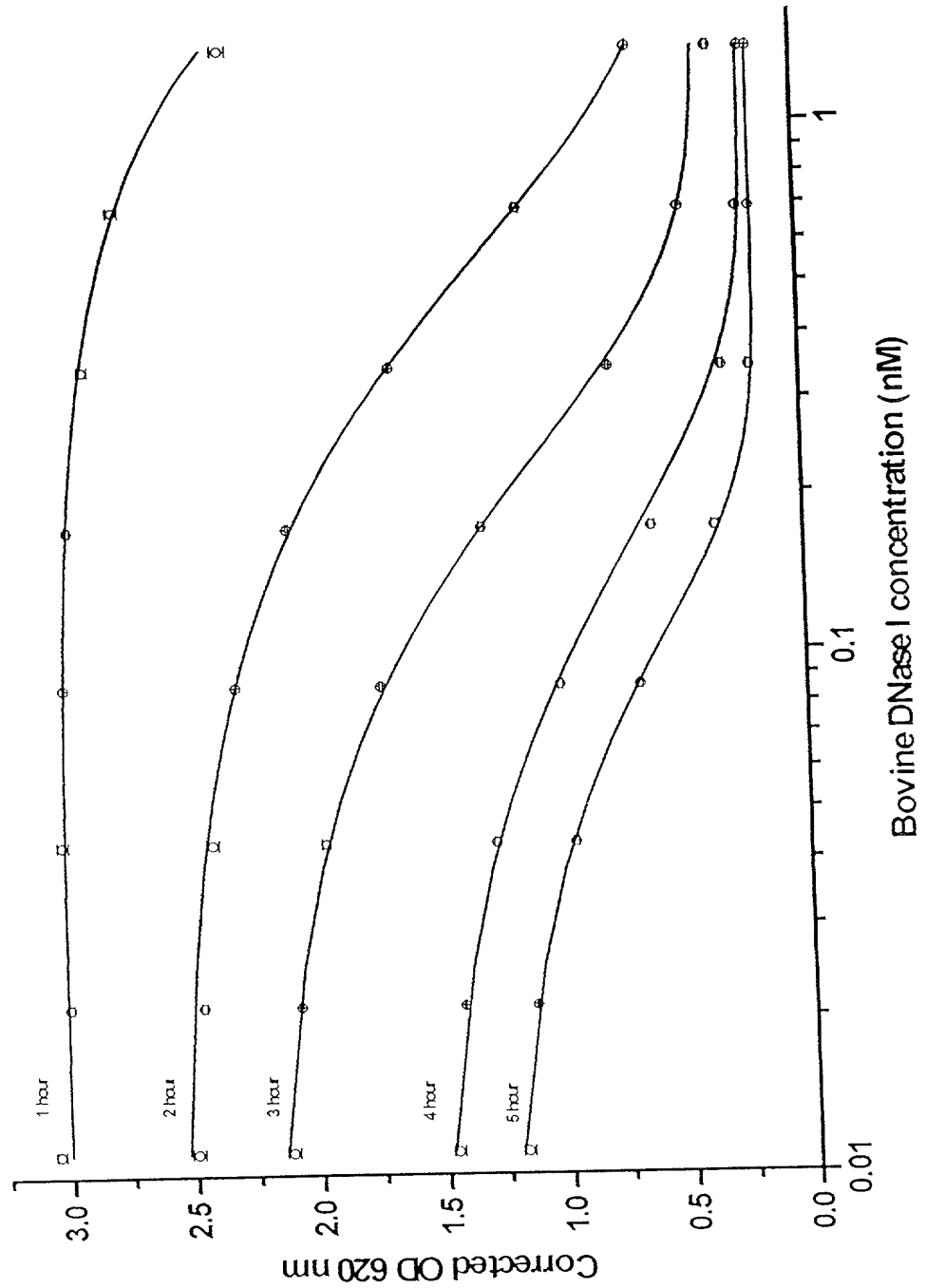
Corrected DNase I activity in transiently expressed humanised human HMFG1-human DNase I constructs

FIG 24
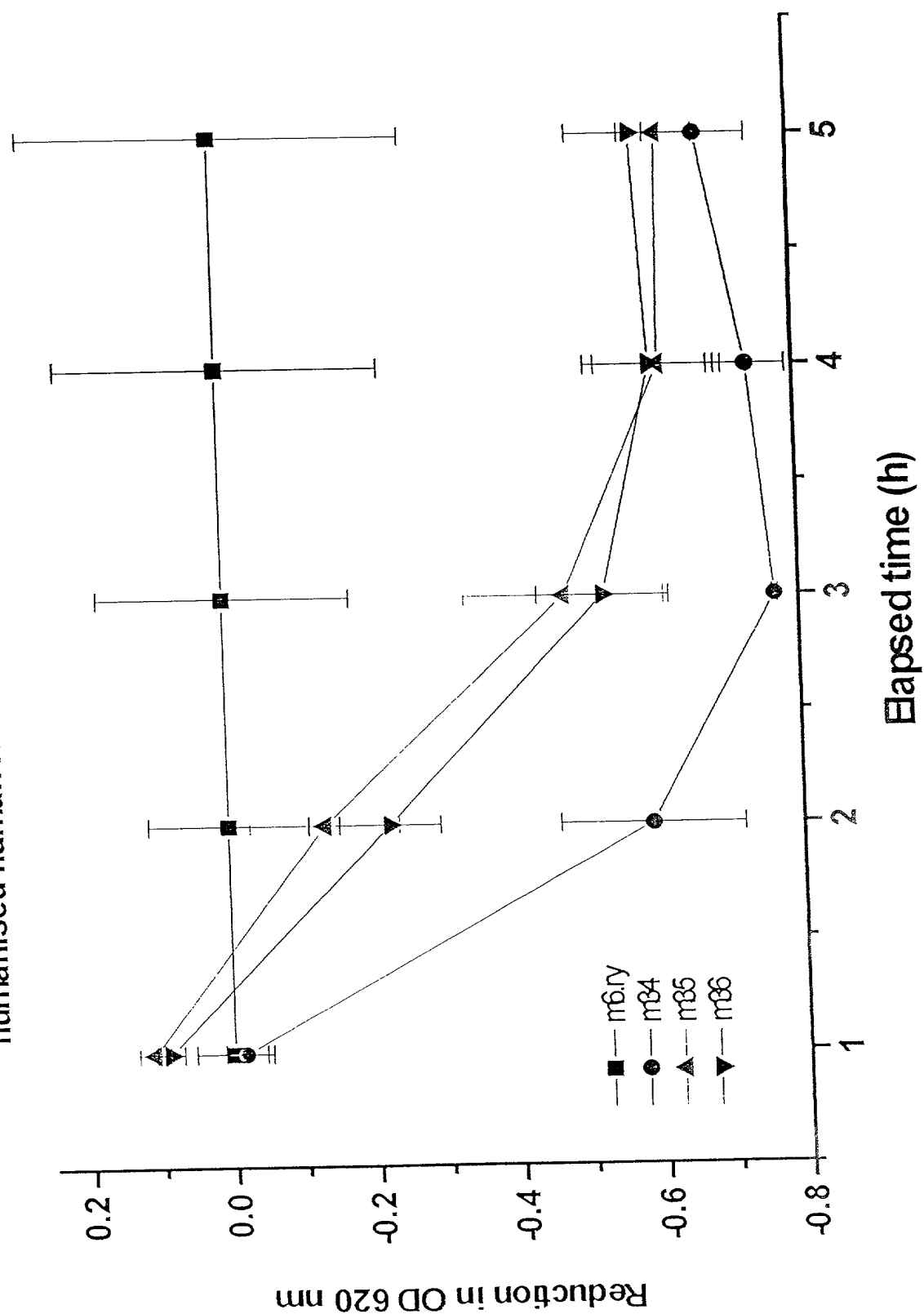
Corrected DNase I activity in transiently expressed humanised HMFG1 F(ab')2-human DNase I fusions
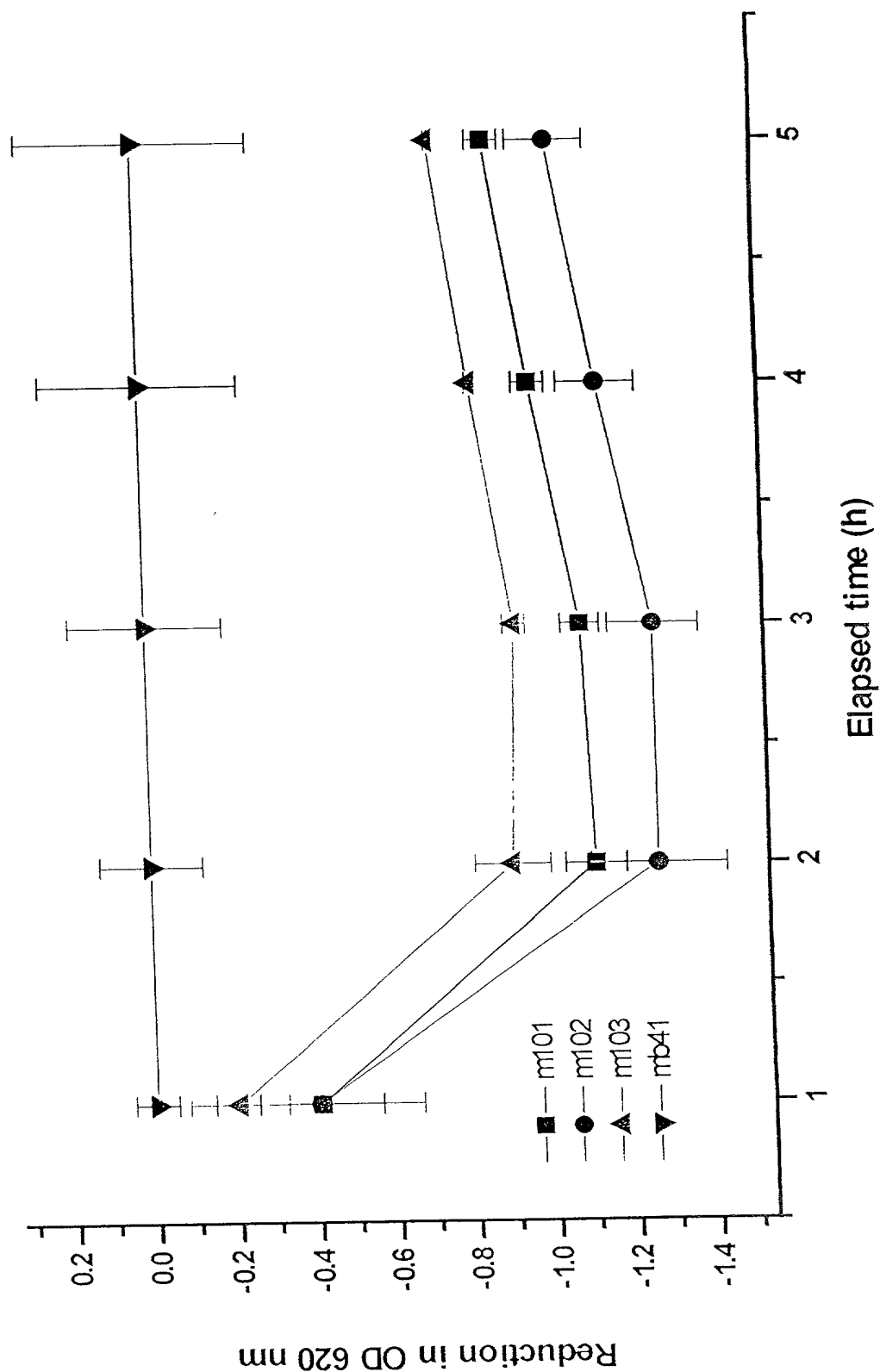
FIG 25

FIG. 26

Cytotoxicity Assay
10,000 cells/Well
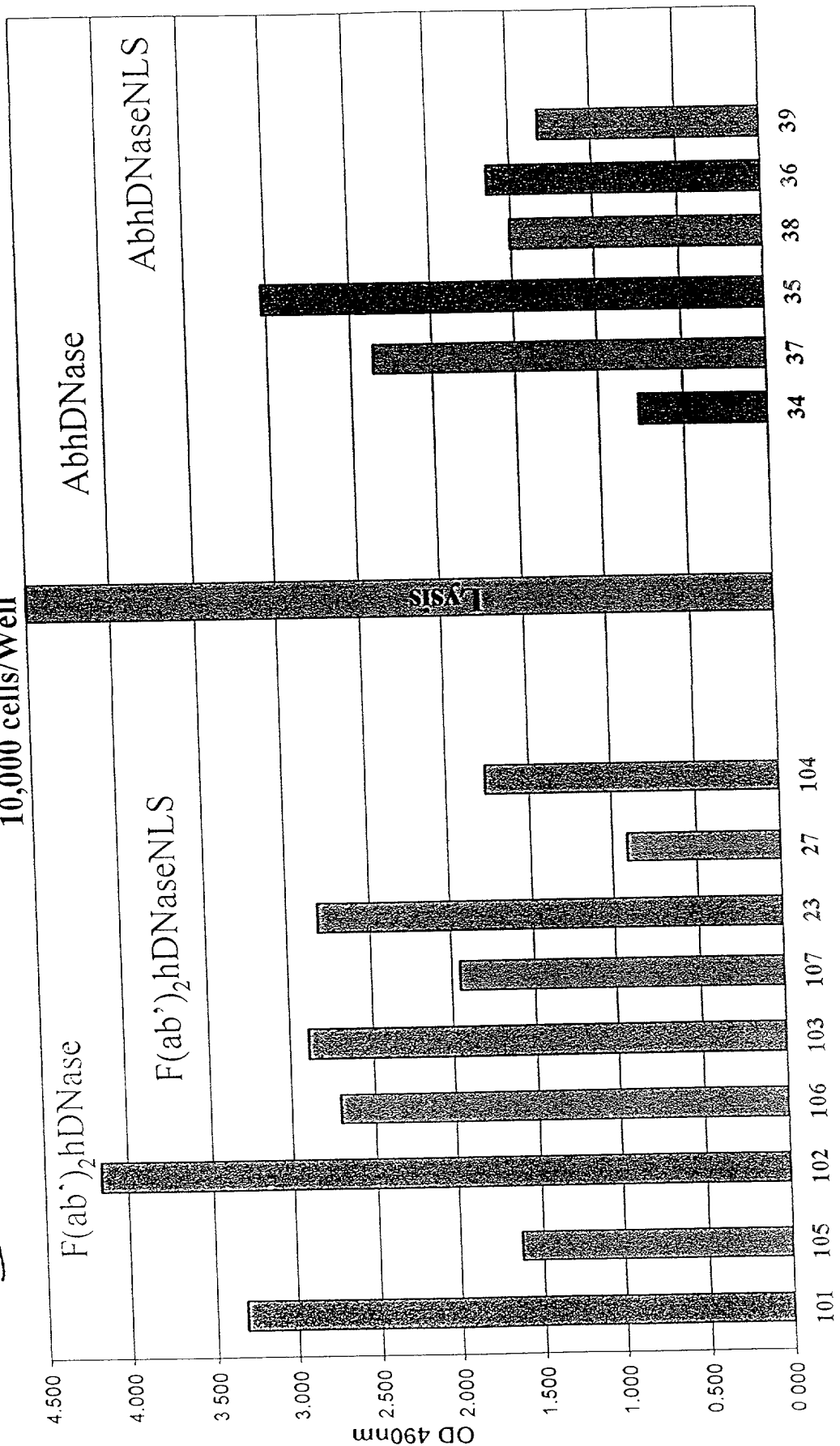
0.097 μg/ml of each construct

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MCF7 cells killed after 1h incubation with 1.35 ng of sample

FIG 27

Figure 28

A — Ab-DNase

hDNase I
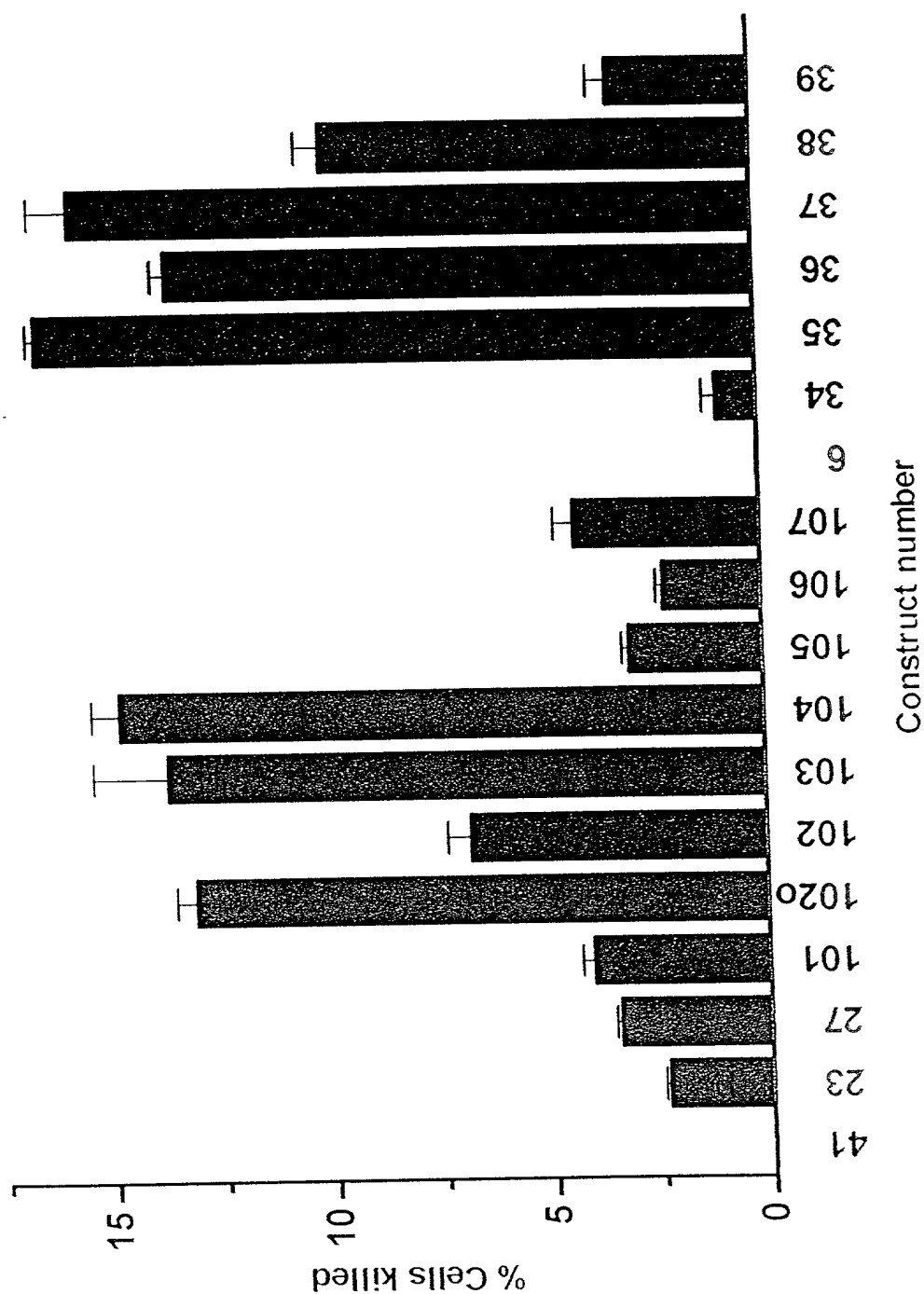
B — Fab-DNase
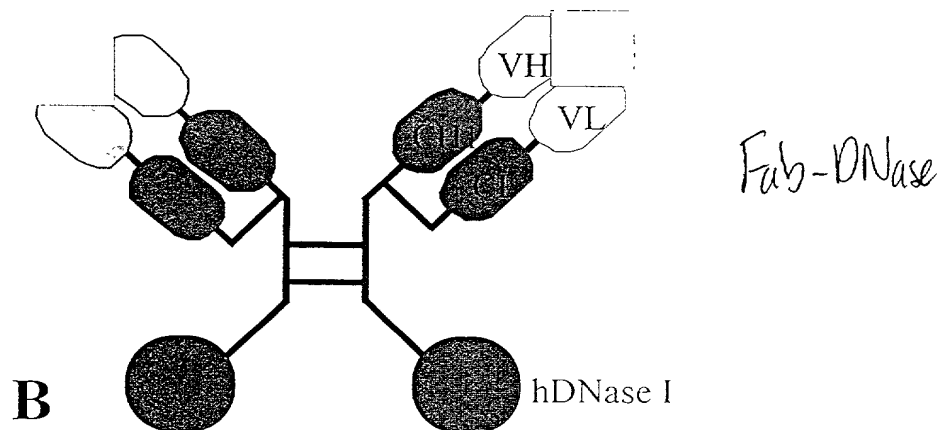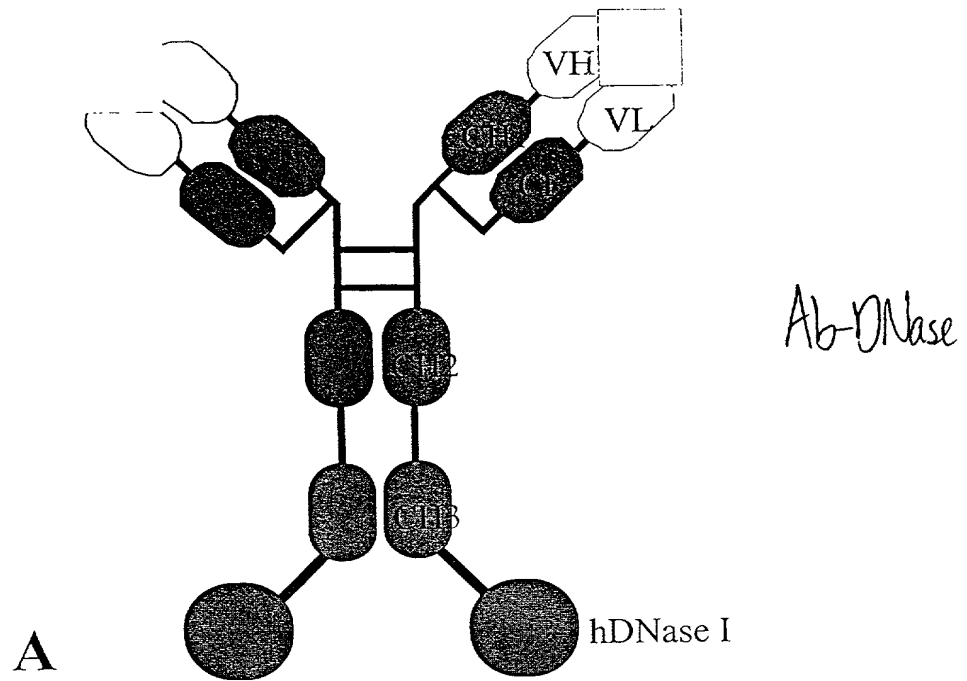
hDNase I
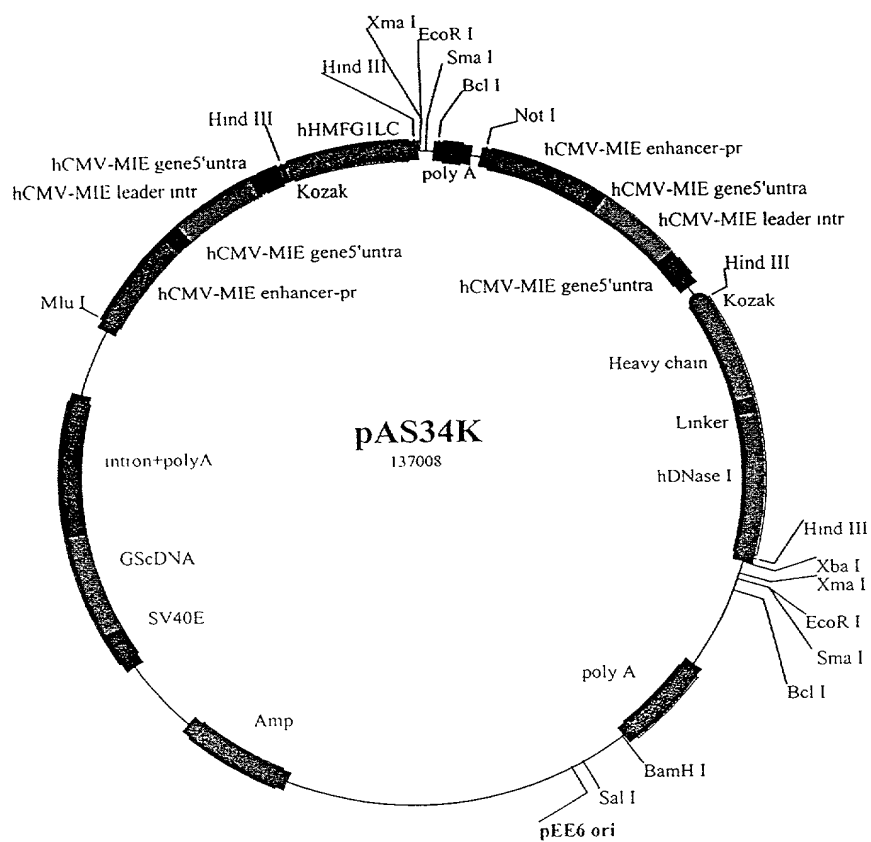
Figure 29

Ab-DNase

Figure 30

Fab-DNase

Figure 31

A

B

A

Figure 32

B

Elution Volume (ml)
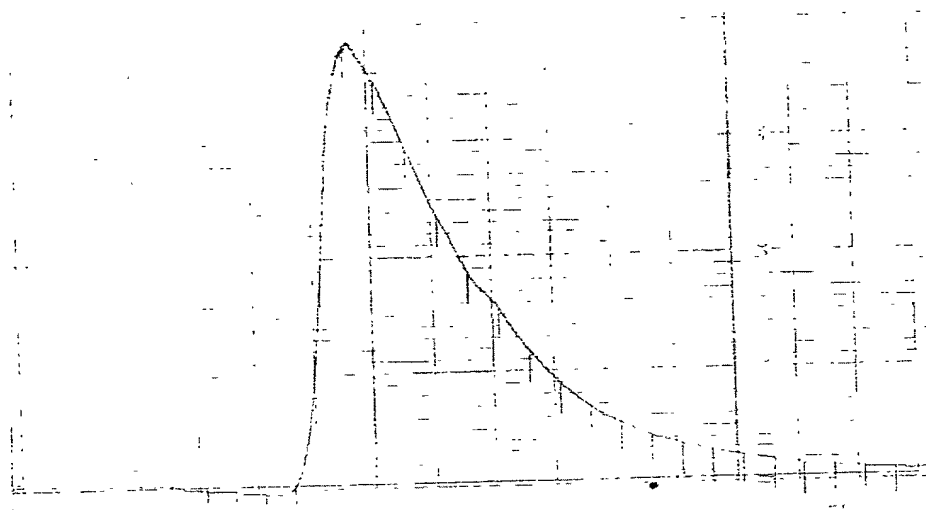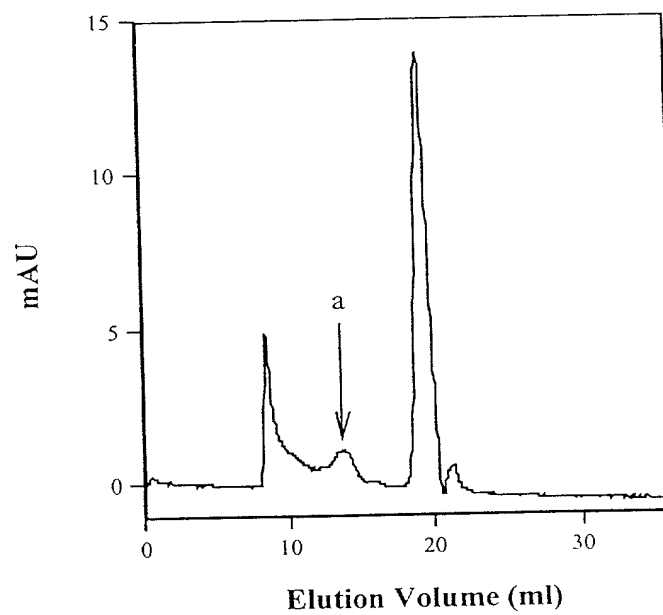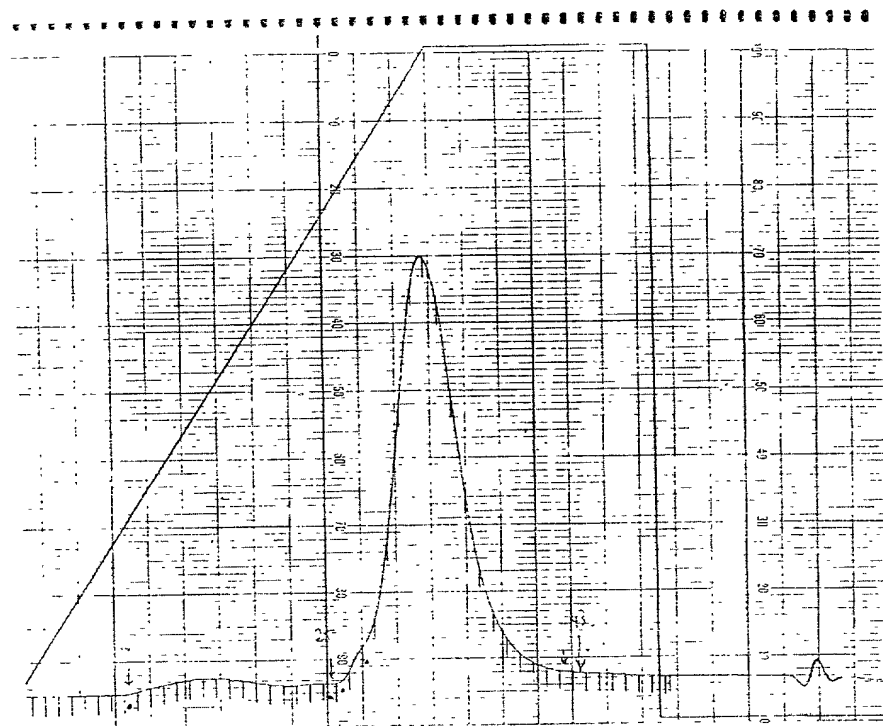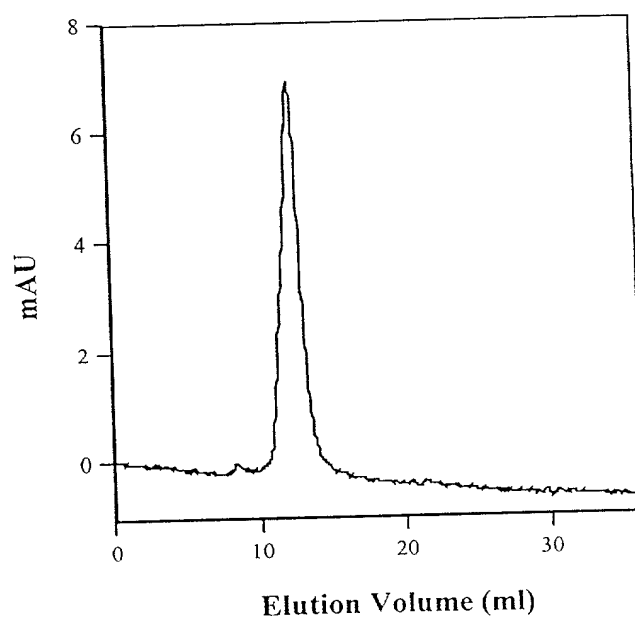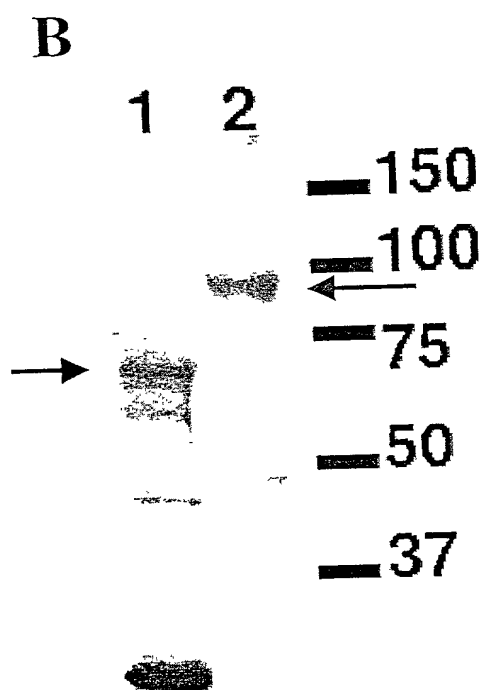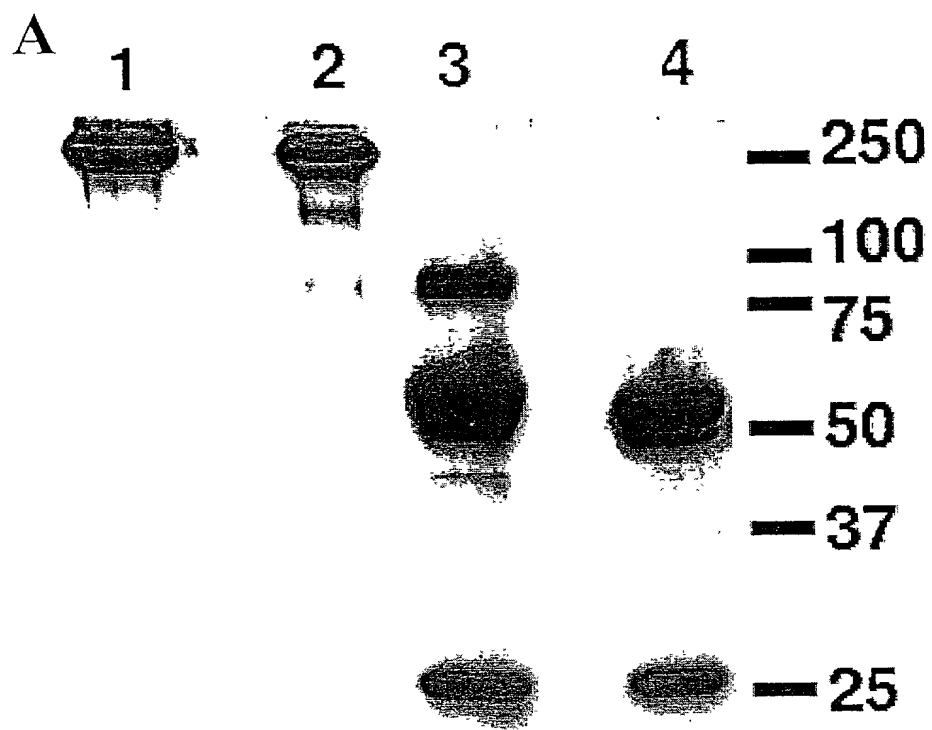
Figure 33

Figure 34

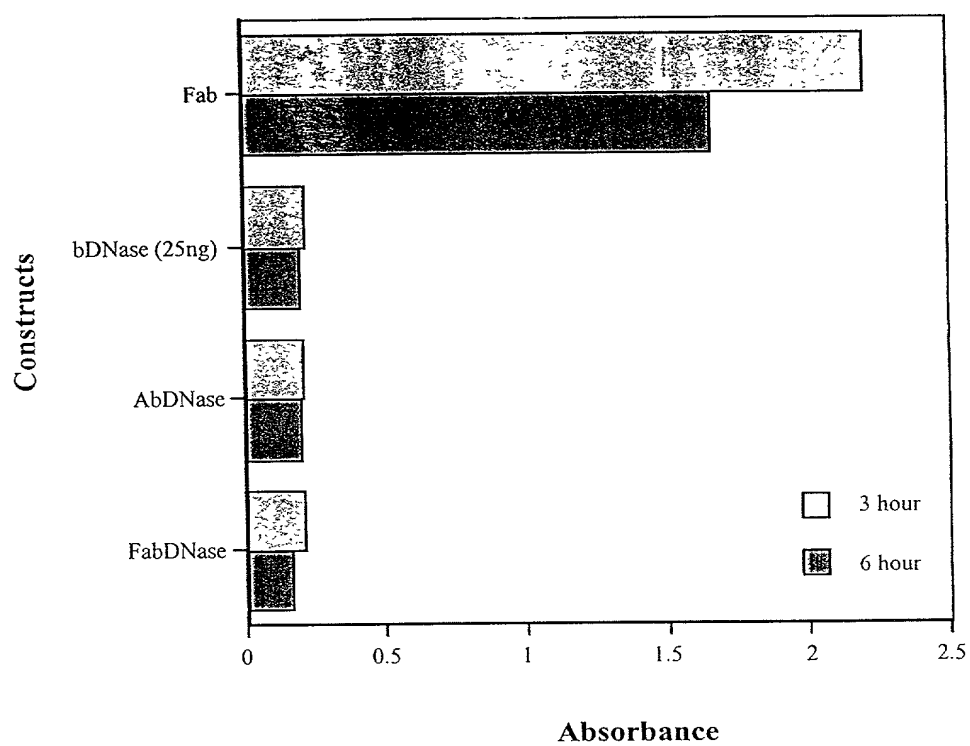# Bovine DNase I standard curves at various time points
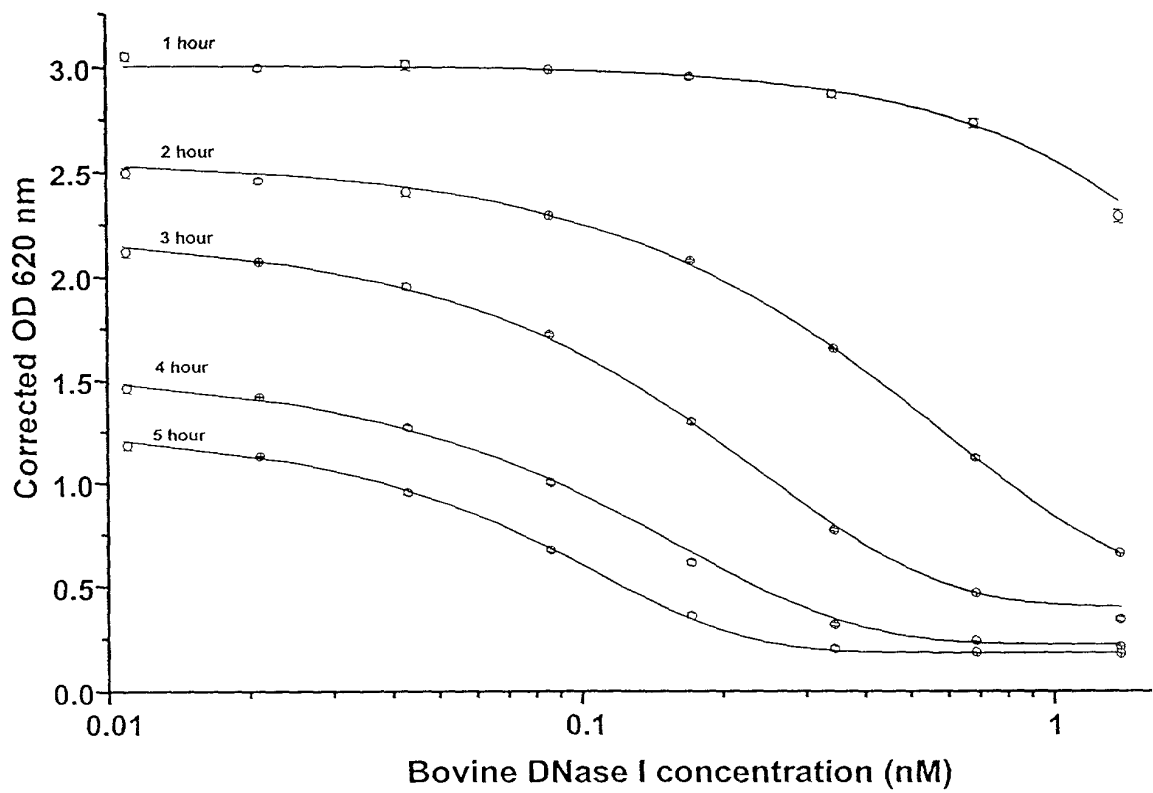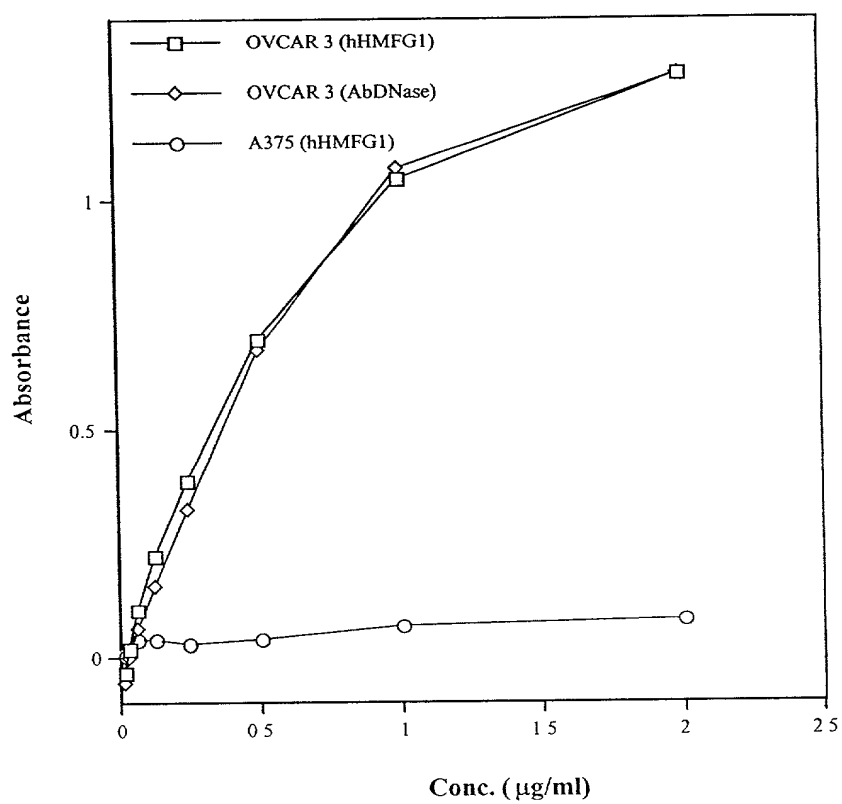

A

Figure 34 – cont.

B

Figure 35

A

Figure 35 – cont.

B